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INTERNATIONALE ANMELDUNG VERÖFFENTLICHT NACH DEM VERTRAG ÜBER DIE  
INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT)

(51) Internationale Patentklassifikation <sup>6</sup> : <b>C07D 493/04, 417/06, 413/06, 277/24</b>		A2	(11) Internationale Veröffentlichungsnummer: <b>WO 99/65913</b>
			(43) Internationales Veröffentlichungsdatum: <b>23. Dezember 1999 (23.12.99)</b>
(21) Internationales Aktenzeichen: <b>PCT/EP99/04244</b>		(81) Bestimmungsstaaten: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO Patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), eurasisches Patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI Patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(22) Internationales Anmeldedatum: <b>18. Juni 1999 (18.06.99)</b>		Veröffentlicht <i>Ohne internationalen Recherchenbericht und erneut zu veröffentlichen nach Erhalt des Berichts.</i>	
(30) Prioritätsdaten: <b>198 26 988.9 18. Juni 1998 (18.06.98) DE</b>			
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(54) Titel: EPOTHILON MINOR CONSTITUENTS			
(54) Bezeichnung: EPOTHILON-NEBENKOMPONENTEN			
(57) Abstract			
The invention relates to compounds which are obtained by fermenting DSM 6773, especially epothilones A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 and K and trans-epothilones C1 and C2.			
(57) Zusammenfassung			
Die Erfindung betrifft Verbindungen, die durch Fermentation von DSM 6773 erhältlich sind, insbesondere Epothilone A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 und K und Trans-Epothilone C1 und C2.			

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### Epothilon-Nebenkomponenten

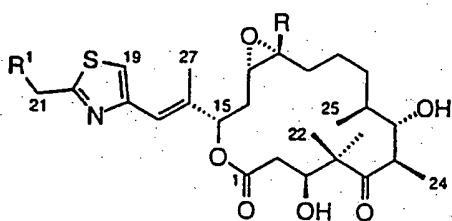
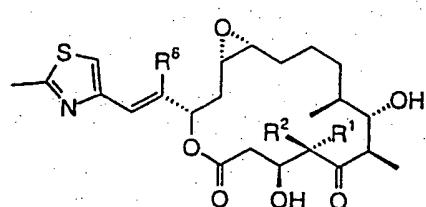
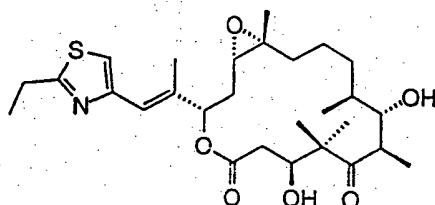
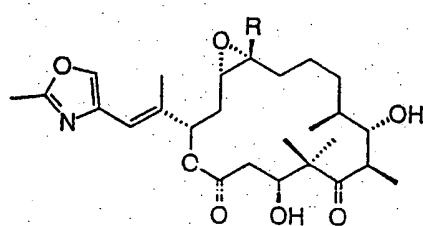
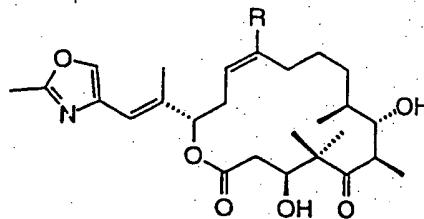
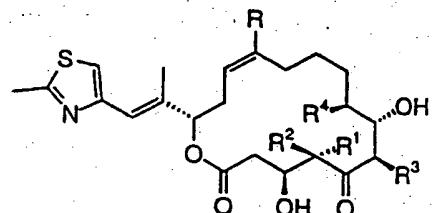
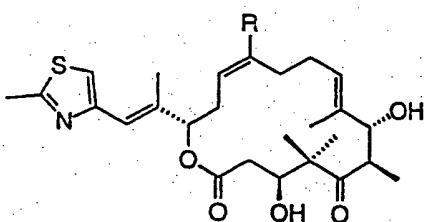
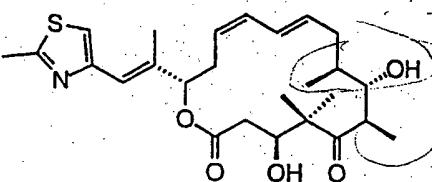
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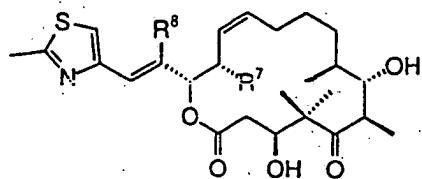
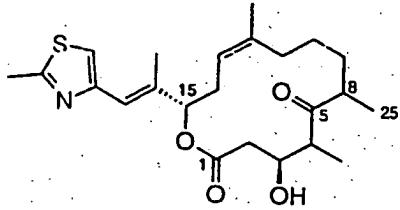
Die Erfindung betrifft Verbindungen, die im vorliegenden Zusammenhang als Epothilon-Nebenkomponenten bezeichnet werden, und zwar Verbindungen 5 bis 13 und 16 bis 39. Diese Verbindungen lassen sich durch Fermentation von DSM 6773 gemäß DE 41 38 042.8 gewinnen.

Kenndaten der erfindungsgemäßen Verbindungen sind im folgenden zusammengestellt.

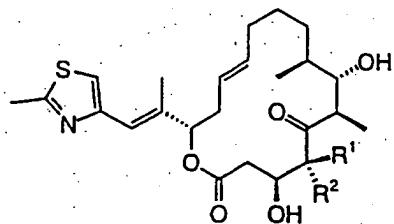
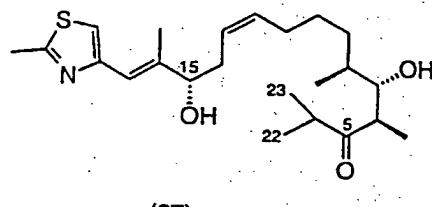
Gewinnung: Die Aufarbeitung eines Rohepothilon-Gemischs, das durch Fermentation von DSM 6773 in einem 900 Liter-Fermentator gewonnen wurde, ist schematisch Fig. 1 bis 2 zu entnehmen.

Aktivitäten: vgl. Tab. 1

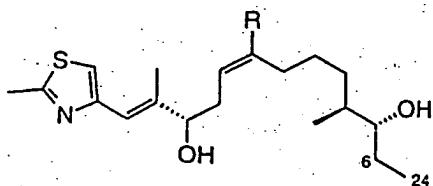
Epothilone A (1) R<sup>1</sup> = H; R = HEpothilone B (2) R<sup>1</sup> = H; R = MeEpothilone E (3) R<sup>1</sup> = OH; R = HEpothilone F (4) R<sup>1</sup> = OH; R = MeEpothilone A<sub>1</sub> (5) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>8</sup> = MeEpothilone A<sub>2</sub> (6) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>8</sup> = MeEpothilone A<sub>8</sub> (7) R<sup>8</sup> = H; R<sup>1</sup>, R<sup>2</sup> = MeEpothilone A<sub>9</sub> (8) R<sup>1</sup> = CH<sub>2</sub>OH; R<sup>2</sup>, R<sup>8</sup> = MeEpothilone B<sub>10</sub> (9)Epothilone G<sub>1</sub> (10) R = HEpothilone G<sub>2</sub> (11) R = MeEpothilone H<sub>1</sub> (12) R = HEpothilone H<sub>2</sub> (13) R = MeEpothilone C (14) R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = HEpothilone D (15) R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup>, R = MeEpothilone C<sub>1</sub> (16) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = HEpothilone D<sub>1</sub> (17) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = MeEpothilone C<sub>2</sub> (18) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = HEpothilone D<sub>2</sub> (19) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = MeEpothilone C<sub>3</sub> (20) R<sup>3</sup> = H; R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup> = Me; R = HEpothilone C<sub>4</sub> (21) R<sup>4</sup> = H; R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> = Me; R = HEpothilone C<sub>5</sub> (22) R = HEpothilone D<sub>5</sub> (23) R = MeEpothilone C<sub>6</sub> (24)

Epothilone C<sub>7</sub> (25) R<sup>7</sup> = OH; R<sup>8</sup> = MeEpothilone C<sub>8</sub> (26) R<sup>8</sup>, R<sup>7</sup> = HEpothilone C<sub>9</sub> (27) R<sup>8</sup> = CH<sub>2</sub>OH; R<sup>7</sup> = H

Epothilone K (36)

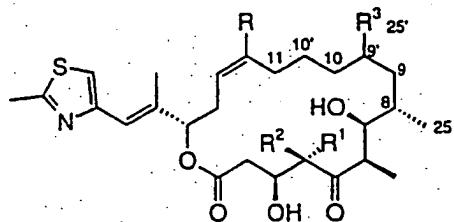
trans-Epothilone C<sub>1</sub> (28) R<sup>1</sup> = H; R<sup>2</sup> = Metrans-Epothilone C<sub>2</sub> (29) R<sup>2</sup> = H; R<sup>1</sup> = Me

(37)



(38) R = H

(39) R = Me

Epothilone I<sub>1</sub> (30) R, R<sup>3</sup> = H; R<sup>1</sup>, R<sup>2</sup> = MeEpothilone I<sub>2</sub> (31) R = H; R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> = MeEpothilone I<sub>3</sub> (32) R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R = MeEpothilone I<sub>4</sub> (33) R<sup>2</sup>, R = H; R<sup>1</sup>, R<sup>3</sup> = MeEpothilone I<sub>5</sub> (34) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>3</sup>, R = MeEpothilone I<sub>6</sub> (35) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>3</sup>, R = Me

**Epothilone A<sub>1</sub> (5):** colorless amorphous solid;  $[\alpha]^{22}_D -69$  (*c* 0.1, MeOH); UV (MeOH)

$\lambda_{\text{max}}$  nm ( $\epsilon$ ) 208 (19600), 247 (13600); IR (KBr)  $\nu_{\text{max}}$  3437, 2959, 2931, 2876, 1732, 1710, 1455, 1259, 978  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  6.95 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.68 (1H, dd, *J* = 4.4, 4.0 Hz, H-15), 4.12 (1H, m, H-3), 3.71 (1H, m, H-7), 3.52 (1H, bs, 7-OH), 3.37 (1H, bd, *J* = 7.5 Hz, 3-OH), 3.21 (1H, dq, *J* = 7.7, 7.0 Hz, H-4), 3.02 (1H, ddd, *J* = 9.2, 4.5, 2.8 Hz, H-13), 2.87 (1H, ddd, *J* = 8.3, 4.5, 3.7 Hz, H-12), 2.78 (1H, dd, *J* = 16.8, 4.3 Hz, H-2a), 2.70 (3H, s, H-21), 2.66 (1H, dq, *J* = 3.9, 7.0 Hz, H-6), 2.65 (1H, dd, *J* = 16.8, 5.2 Hz, H-2b), 2.16 (1H, ddd, *J* = 15.4, 4.4, 2.8 Hz, H-14a), 2.12 (3H, bs, H-27), 1.91 (1H, ddd, *J* = 15.4, 9.2, 4.0 Hz, H-14b), 1.63 (1H, m, H-10a), 1.62 (2H, m, H-11), 1.59 (1H, m, H-9a), 1.52 (1H, m, H-10b), 1.39 (1H, m, H-8), 1.35 (1H, m, H-9b), 1.211 (3H, d, *J* = 7.0 Hz, H-23), 1.207 (3H, d, *J* = 7.0 Hz, H-24), 0.89 (3H, d, *J* = 6.9 Hz, H-25); EIMS *m/z* 479 [M]<sup>+</sup> (21), 322 (31), 306 (65), 304 (47), 168 (45), 166 (73), 164 (100), 151 (30), 140 (35); HREIMS *m/z* 479.2317 (calcd. for C<sub>27</sub>H<sub>41</sub>NO<sub>5</sub>S, 479.2342).

**Epothilone A<sub>2</sub> (6):** colorless amorphous solid;  $[\alpha]^{22}_D +12.0$  (*c* 1.0, MeOH); UV (MeOH)

$\lambda_{\text{max}}$  nm ( $\epsilon$ ) 210 (15100), 248 (15500); IR (KBr)  $\nu_{\text{max}}$  3438, 2963, 2929, 2875, 1734, 1706, 1458, 1262, 981  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  6.98 (1H, s, H-19), 6.63 (1H, bs, H-17), 5.40 (1H, dd, *J* = 8.3, 3.4 Hz, H-15), 4.26 (1H, ddd, *J* = 8.5, 4.8, 4.7 Hz, H-3), 3.85 (1H, dd, *J* = 7.9,

2.6 Hz, H-7), 3.54 (1H, bs, 3-OH), 3.09 (1H, dq,  $J = 4.8, 7.0$  Hz, H-4), 3.01 (1H, ddd,  $J = 8.3, 4.8, 4.6$  Hz, H-13), 2.98 (1H, dq,  $J = 7.9, 7.0$  Hz, H-6), 2.89 (1H, ddd,  $J = 6.7, 4.6, 4.4$  Hz, H-12), 2.68 (3H, s, H-21), 2.60 (1H, dd,  $J = 15.1, 8.5$  Hz, H-2a), 2.52 (1H, bs, 7-OH), 2.50 (1H, dd,  $J = 15.1, 4.7$  Hz, H-2b), 2.18 (1H, ddd,  $J = 15.0, 4.8, 3.4$  Hz, H-14a), 2.11 (3H, d,  $J = 1.3$  Hz, H-27), 1.82 (1H, ddd,  $J = 15.0, 8.3, 8.1$  Hz, H-14b), 1.63 (1H, m, H-8), 1.61 (2H, m, H-11a and H-10a), 1.46 (1H, m, H-11b), 1.39 (2H, m, H-9), 1.31 (1H, m, H-10b), 1.22 (3H, d,  $J = 7.0$  Hz, H-24), 1.15 (3H, d,  $J = 7.0$  Hz, H-22), 1.01 (3H, d,  $J = 6.9$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  216.2 (s, C-5), 170.1 (s, C-1), 164.9 (s, C-20), 152.0 (s, C-18), 137.0 (s, C-16), 120.3 (d, C-17), 116.5 (d, C-19), 76.7 (d, C-15), 75.6 (d, C-7), 69.1 (d, C-3), 57.1 (d, C-12), 54.3 (d, C-13), 50.3 (d, C-4), 49.6 (d, C-6), 39.4 (t, C-2), 35.5 (d, C-8), 32.2 (t, C-14), 29.6 (t, C-9), 27.6 (t, C-11), 23.9 (t, C-10), 19.2 (q, C-21), 18.0 (q, C-25), 15.6 (q, C-27), 13.9 (q, C-24), 12.4 (q, C-22); EIMS  $m/z$  479 [M] $^+$  (18), 322 (38), 306 (78), 304 (59), 168 (48), 166 (96), 164 (100), 151 (33), 140 (38); HREIMS  $m/z$  479.2318 (calcd. for  $\text{C}_{27}\text{H}_{41}\text{NO}_5\text{S}$ , 479.2342).

Epothilone A<sub>8</sub> (7): colorless amorphous solid;  $[\alpha]^{22}_D -76.2$  ( $c$  1.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 210 (15300), 248 (15500); IR (KBr)  $\nu_{\text{max}}$  3440, 2967, 2932, 2876, 1736, 1691, 1467, 1252, 979  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.95 (1H, s, H-19), 6.64 (1H, dd,  $J = 15.6, 0.9$  Hz, H-17), 6.52 (1H, dd,  $J = 15.6, 6.6$  Hz, H-16), 5.68 (1H, dddd,  $J = 7.8, 6.6, 3.2, 0.9$  Hz, H-15), 4.11 (1H, ddd,  $J = 10.1, 6.6, 3.5$  Hz, H-3), 3.78 (1H, ddd,  $J = 5.2, 3.2, 3.2$  Hz, H-7), 3.66 (1H, d,  $J = 6.6$  Hz, 3-OH), 3.23 (1H, dq,  $J = 5.2, 6.9$  Hz, H-6), 3.08 (1H, ddd,  $J = 7.3, 5.5, 4.1$  Hz, H-13), 2.90 (1H, ddd,  $J = 6.6, 4.6, 4.1$  Hz, H-12), 2.69 (3H, s, H-21), 2.52 (1H, dd,  $J = 14.7, 10.1$  Hz, H-2a), 2.44 (1H, bd,  $J = 3.2$  Hz, 7-OH), 2.41 (1H, dd,  $J = 14.7, 3.5$  Hz, H-2b), 2.10

(1H, ddd,  $J = 15.0, 5.5, 3.2$  Hz, H-14a), 1.90 (1H, ddd,  $J = 15.0, 7.8, 7.3$  Hz, H-14b), 1.71 (1H, m, H-8), 1.65 (1H, m, H-11a), 1.50 (1H, m, H-10a), 1.47 (1H, m, H-11b), 1.40 (2H, m, H-9), 1.39 (1H, m, H-10b), 1.33 (3H, s, H-23), 1.16 (3H, d,  $J = 6.9$  Hz, H-24), 1.08 (3H, s, H-22), 0.98 (3H, d,  $J = 7.0$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  220.3 (s, C-5), 170.7 (s, C-1), 166.5 (s, C-20), 152.2 (s, C-18), 128.4 (d, C-16), 125.9 (d, C-17), 116.4 (d, C-19), 75.0 (d, C-7), 73.6 (d, C-3), 72.7 (d, C-15), 57.3 (d, C-12), 54.1 (d, C-13), 52.6 (s, C-4), 43.8 (d, C-6), 38.9 (t, C-2), 36.3 (d, C-8), 32.5 (t, C-14), 30.3 (t, C-9), 26.7 (t, C-11), 24.0 (t, C-10), 21.3 (q, C-23), 21.0 (q, C-22), 19.3 (q, C-21), 17.1 (q, C-25), 14.5 (q, C-24); EIIMS  $m/z$  479 [M]<sup>+</sup> XXX; HRDCIIMS  $m/z$  480.2401 (calcd. for  $\text{C}_{25}\text{H}_{38}\text{NO}_6\text{S}$ , 480.2401).

Epothilone A<sub>9</sub> (8): colorless amorphous solid;  $[\alpha]^{22}_D -37.6$  ( $c$  0.5, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 211 (15500), 253 (14100); IR (KBr)  $\nu_{\text{max}}$  3423, 2965, 2932, 2877, 1736, 1690, 1463, 1249, 1014, 979  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.10 (1H, s, H-19), 6.72 (1H, dd,  $J = 10.7, 4.3$  Hz, 27-OH), 6.60 (1H, bs, H-17), 5.69 (1H, dd,  $J = 11.6, 2.0$  Hz, H-15), 5.59 (1H, d,  $J = 6.6$  Hz, 3-OH), 4.49 (1H, ddd,  $J = 12.9, 4.3, 1.2$  Hz, H-27a), 4.27 (1H, ddd,  $J = 11.6, 6.6, 2.9$  Hz, H-3), 4.11 (1H, ddd,  $J = 12.9, 10.7, 1.0$  Hz, H-27b), 3.71 (1H, ddd,  $J = 4.8, 3.0, 2.8$  Hz, H-7), 3.17 (1H, dq,  $J = 3.0, 6.8$  Hz, H-6), 3.04 (1H, ddd,  $J = 9.7, 3.6, 2.2$  Hz, H-13), 2.93 (1H, bs, 7-OH), 2.91 (1H, ddd,  $J = 9.7, 3.6, 2.7$  Hz, H-12), 2.72 (3H, s, H-21), 2.48 (1H, dd,  $J = 14.2, 11.6$  Hz, H-2a), 2.11 (1H, dd,  $J = 14.2, 2.9$  Hz, H-2b), 2.03 (1H, ddd,  $J = 14.7, 2.2, 2.0$  Hz, H-14a), 1.86 (1H, m, H-11a), 1.85 (1H, m, H-14b), 1.79 (1H, m, H-8), 1.52 (1H, m, H-10a), 1.37 (3H, m, H-9 and H-10b), 1.37 (3H, s, H-23), 1.36 (1H, m, H-11b), 1.19 (3H, d,  $J = 6.8$  Hz, H-24), 1.02 (3H, d,  $J = 7.1$  Hz, H-25), 1.00 (3H, s, H-22);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  220.5 (s, C-5),

170.2 (s, C-1), 167.5 (s, C-20), 150.7 (s, C-18), 138.9 (s, C-16), 125.2 (d, C-17), 119.5 (d, C-19), 76.7 (d, C-15), 73.4 (d, C-7), 70.4 (d, C-3), 57.7 (d, C-12), 57.2 (t, C-27), 55.3 (d, C-13), 54.2 (s, C-4), 41.3 (d, C-6), 40.7 (t, C-2), 37.5 (d, C-8), 31.8 (t, C-14), 31.2 (t, C-9), 28.0 (t, C-11), 23.7 (q, C-23), 23.2 (t, C-10), 19.2 (q, C-21), 16.8 (q, C-22), 15.8 (q, C-25), 13.5 (q, C-24); EIMS  $m/z$  509 [M]<sup>+</sup> (9), 491 (4), 322 (28), 321 (25), 180 (45), 167 (40), 166 (100), 165 (49), 154 (47), 138 (33); HREIMS  $m/z$  509.2467 (calcd. for  $C_{26}H_{39}NO_7S$ , 509.2447).

Epothilone B<sub>10</sub> (9): colorless amorphous solid;  $[\alpha]^{22}_D$  -27 (*c* 0.15, MeOH); UV (MeOH)  $\lambda_{max}$  nm ( $\epsilon$ ) 212 (15800), 247 (12500); IR (KBr)  $\nu_{max}$  3434, 2962, 2930, 2876, 2858, 1733, 1692, 1461, 1259, 1052, 981 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$  6.99 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.42 (1H, dd, *J* = 8.0, 3.0 Hz, H-15), 4.25 (1H, ddd, *J* = 9.5, 6.3, 2.8 Hz, H-3), 4.23 (1H, bs, 3-OH), 3.77 (1H, ddd, *J* = 4.0, 3.9, 3.8 Hz, H-7), 3.30 (1H, dq, *J* = 4.0, 6.9 Hz, H-6), 3.01 (2H, q, *J* = 7.6 Hz, H-21), 2.81 (1H, dd, *J* = 7.7, 4.6 Hz, H-13), 2.68 (1H, bs, 7-OH), 2.54 (1H, dd, *J* = 13.9, 9.5 Hz, H-2a), 2.36 (1H, dd, *J* = 13.9, 2.8 Hz, H-2b), 2.11 (1H, ddd, *J* = 15.3, 4.6, 3.0 Hz, H-14a), 2.09 (3H, s, H-27), 1.91 (1H, ddd, *J* = 15.3, 8.0, 7.7 Hz, H-14b), 1.74 (1H, m, H-8), 1.73 (1H, m, H-11a), 1.51 (1H, m, H-10a), 1.41 (1H, m, H-11b), 1.39 (3H, t, *J* = 7.6 Hz, H-28), 1.38 (3H, m, H-9 and H-10b), 1.37 (3H, s, H-23), 1.28 (3H, s, H-26), 1.17 (3H, d, *J* = 6.9 Hz, H-24), 1.09 (3H, s, H-22), 1.01 (3H, d, *J* = 7.0 Hz, H-25); EIMS  $m/z$  521 [M]<sup>+</sup> (22), 449 (7), 350 (18), 334 (57), 248 (16), 234 (27), 196 (41), 182 (59), 180 (96), 178 (100), 166 (44), 154 (44); HREIMS  $m/z$  521.2808 (calcd. for  $C_{28}H_{43}NO_6S$ , 521.2811).

Epothilone G<sub>1</sub> (10): colorless amorphous solid;  $[\alpha]^{22}_D$  -39.7 (*c* 1.0, MeOH); UV (MeOH)  $\lambda_{max}$  nm ( $\epsilon$ ) 203 (15200), 236 (15100); IR (KBr)  $\nu_{max}$  3456, 2962, 2933, 2876, 1736,

1691, 1585, 1466, 1262, 980  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.47 (1H, s, H-19), 6.33 (1H, bs, H-17), 5.42 (1H, dd,  $J$  = 8.3, 2.9 Hz, H-15), 4.11 (1H, ddd,  $J$  = 10.1, 6.1, 3.4 Hz, H-3), 3.78 (1H, bddd,  $J$  = 5.2, 3.5, 3.5 Hz, H-7), 3.63 (1H, bd,  $J$  = 6.1 Hz, 3-OH), 3.21 (1H, dq,  $J$  = 5.2, 7.0 Hz, H-6), 3.00 (1H, ddd,  $J$  = 7.7, 4.8, 4.2 Hz, H-13), 2.88 (1H, ddd,  $J$  = 7.1, 4.2, 4.2 Hz, H-12), 2.53 (1H, dd,  $J$  = 14.8, 10.1 Hz, H-2a), 2.51 (1H, bd,  $J$  = 3.5 Hz, 7-OH), 2.43 (1H, dd,  $J$  = 14.8, 3.4 Hz, H-2b), 2.43 (3H, s, H-21), 2.07 (1H, ddd,  $J$  = 15.1, 4.8, 2.9 Hz, H-14a), 1.99 (3H, d,  $J$  = 1.3 Hz, H-27), 1.86 (1H, ddd,  $J$  = 15.1, 8.3, 7.7 Hz, H-14b), 1.71 (1H, m, H-8), 1.69 (1H, m, H-11a), 1.53 (1H, m, H-10a), 1.42 (1H, m, H-11b), 1.40 (3H, m, H-9 and H-10b), 1.34 (3H, s, H-23), 1.16 (3H, d,  $J$  = 7.0 Hz, H-24), 1.09 (3H, s, H-22), 0.99 (3H, d,  $J$  = 6.9 Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  220.1 (s, C-5), 170.5 (s, C-1), 161.0 (s, C-20), 137.4 (s, C-18), 136.7 (s, C-16), 135.9 (d, C-19), 116.4 (d, C-17), 76.4 (d, C-15), 74.9 (d, C-7), 73.7 (d, C-3), 57.4 (d, C-12), 54.4 (d, C-13), 52.6 (s, C-4), 43.8 (d, C-6), 38.8 (t, C-2), 36.2 (d, C-8), 31.4 (t, C-14), 30.4 (t, C-9), 27.0 (t, C-11), 23.9 (t, C-10), 21.3 (q, C-23), 21.2 (q, C-22), 17.2 (q, C-25), 15.8 (q, C-27), 14.4 (q, C-24), 13.8 (q, C-21); EIMS  $m/z$  477 [M]<sup>+</sup> (4), 405 (7), 290 (40), 152 (39), 150 (100), 148 (23), 124 (23); HREIMS  $m/z$  477.2684 (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_7$ , 477.2727).

**Epothilone G<sub>2</sub>** (11): colorless amorphous solid;  $[\alpha]^{22}_D$  -22.6 (*c* 1.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 202 (21500), 236 (14800); IR (KBr)  $\nu_{\text{max}}$  3456, 2965, 2934, 2877, 1737, 1690, 1586, 1464, 1250, 980  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.48 (1H, s, H-19), 6.33 (1H, bs, H-17), 5.43 (1H, dd,  $J$  = 7.1, 3.6 Hz, H-15), 4.12 (1H, ddd,  $J$  = 9.9, 6.4, 3.4 Hz, H-3), 3.77 (1H, ddd,  $J$  = 4.7, 4.4, 4.1 Hz, H-7), 3.83 (1H, bd,  $J$  = 6.4 Hz, 3-OH), 3.30 (1H, dq,  $J$  = 4.7, 6.9

Hz, H-6), 2.78 (1H, dd,  $J = 7.0, 5.4$  Hz, H-13), 2.54 (1H, dd,  $J = 14.3, 9.9$  Hz, H-2a), 2.51 (1H, bd,  $J = 4.1$  Hz, 7-OH), 2.44 (3H, s, H-21), 2.40 (1H, dd,  $J = 14.3, 3.4$  Hz, H-2b), 2.03 (1H, ddd,  $J = 15.2, 5.4, 3.6$  Hz, H-14a), 2.00 (3H, d,  $J = 1.3$  Hz, H-27), 1.92 (1H, ddd,  $J = 15.1, 7.1, 7.0$  Hz, H-14b), 1.71 (1H, m, H-8), 1.68 (1H, m, H-11a), 1.51 (1H, m, H-10a), 1.42 (1H, m, H-11b), 1.39 (3H, m, H-9 and H-10b), 1.35 (3H, s, H-23), 1.26 (3H, s, H-26), 1.16 (3H, d,  $J = 6.9$  Hz, H-24), 1.07 (3H, s, H-22), 0.99 (3H, d,  $J = 7.0$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  220.7 (s, C-5), 170.5 (s, C-1), 161.0 (s, C-20), 137.4 (s, C-18), 136.5 (s, C-16), 135.9 (d, C-19), 116.3 (d, C-17), 76.6 (d, C-15), 74.6 (d, C-7), 73.5 (d, C-3), 61.3 (s, C-12), 61.1 (d, C-13), 52.7 (s, C-4), 43.4 (d, C-6), 39.0 (t, C-2), 36.5 (d, C-8), 32.0 (t, C-11), 31.8 (t, C-14), 30.8 (t, C-9), 22.8 (t, C-10), 22.9 (q, C-26), 21.0 (q, C-23), 20.8 (q, C-22), 17.2 (q, C-25), 15.9 (q, C-27), 14.1 (q, C-24), 13.8 (q, C-21); EIIMS  $m/z$  491[M]<sup>+</sup> (21), 419 (6), 320 (18), 304 (39), 166 (42), 152 (57), 150 (100), 149 (44), 148 (58), 124 (35), 109 (33); HREIMS  $m/z$  491.2878 (calcd. for  $\text{C}_{27}\text{H}_{41}\text{NO}_7$ , 491.2883).

Epothilone H<sub>1</sub> (12): colorless amorphous solid;  $[\alpha]^{22}_D -84.2$  ( $c$  0.2, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 203 (19600), 237 (12000); IR (KBr)  $\nu_{\text{max}}$  3436, 2933, 2880, 2860, 1734, 1688, 1585, 1251, 1007 cm<sup>-1</sup>;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  7.47 (1H, s, H-19), 6.31 (1H, bs, H-17), 5.43 (1H, ddd,  $J = 10.6, 10.2, 4.5$  Hz, H-12), 5.36 (1H, dddd,  $J = 10.6, 9.6, 5.0, 1.3$  Hz, H-13), 5.30 (1H, dd,  $J = 9.9, 2.0$  Hz, H-15), 4.16 (1H, ddd,  $J = 11.2, 5.3, 2.8$  Hz, H-3), 3.73 (1H, ddd,  $J = 3.9, 2.5, 2.3$  Hz, H-7), 3.12 (1H, dq,  $J = 2.3, 6.9$  Hz, H-6), 2.92 (1H, d,  $J = 2.5$  Hz, 7-OH), 2.91 (1H, d,  $J = 5.3$  Hz, 7-OH), 2.66 (1H, ddd,  $J = 15.1, 9.9, 9.6$  Hz, H-14a), 2.50 (1H, dd,  $J = 15.4, 11.2$  Hz, H-2a), 2.43 (3H, s, H-21), 2.37 (1H, dd,  $J = 15.4, 2.8$  Hz, H-2b), 2.23

(1H, m, H-14b), 2.18 (1H, m, H-11a), 2.01 (1H, m, H-11b), 2.08 (3H, d,  $J = 1.3$  Hz, H-27), 1.74 (1H, m, H-8), 1.65 (1H, m, H-10a), 1.33 (1H, m, H-9a), 1.31 (3H, s, H-23), 1.19 (1H, m, H-10b), 1.18 (1H, m, H-9b), 1.17 (3H, d,  $J = 6.9$  Hz, H-24), 1.08 (3H, s, H-22), 0.99 (3H, d,  $J = 7.1$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIIMS  $m/z$  461 [M]<sup>+</sup> (6), 310 (5), 274 (10), 273 (7), 171 (63), 152 (100), 148 (18), 111 (15); HREIMS  $m/z$  461.2743 (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_6$ , 461.2777).

**Epothilone H<sub>2</sub> (13):** colorless amorphous solid;  $[\alpha]^{22}_D -44.4$  ( $c$  0.25, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 203 (14500), 236 (12200); IR (KBr)  $\nu_{\max}$  3436, 2967, 2935, 2880, 1734, 1690, 1586, 1251, 1007 cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.46 (1H, s, H-19), 6.30 (1H, bs, H-17), 5.23 (1H, dd,  $J = 9.8$ , 2.1 Hz, H-15), 5.12 (1H, dd,  $J = 10.1$ , 5.3 Hz, H-13), 4.20 (1H, ddd,  $J = 10.8$ , 5.7, 2.9 Hz, H-3), 3.71 (1H, ddd,  $J = 3.8$ , 2.6, 2.6 Hz, H-7), 3.14 (1H, dq,  $J = 2.6$ , 6.9 Hz, H-6), 2.93 (d,  $J = 5.7$  Hz, 3-OH), 2.90 (1H, bd,  $J = 2.6$  Hz, 7-OH), 2.62 (1H, ddd,  $J = 15.1$ , 9.8, 9.8 Hz, H-14a), 2.46 (1H, dd,  $J = 15.1$ , 10.8 Hz, H-2a), 2.43 (3H, s, H-21), 2.32 (1H, dd,  $J = 15.1$ , 2.9 Hz, H-2b), 2.29 (1H, m, H-11a), 2.19 (1H, bd,  $J = 15.1$  Hz, H-14b), 1.97 (3H, d,  $J = 1.3$  Hz, H-27), 1.87 (1H, m, H-11b), 1.73 (1H, m, H-8), 1.67 (1H, m, H-10a), 1.65 (3H, bs, H-26), 1.32 (3H, s, H-23), 1.26 (2H, m, H-9), 1.24 (1H, m, H-10b), 1.18 (3H, d,  $J = 6.9$  Hz, H-24), 1.07 (3H, s, H-22), 1.00 (3H, d,  $J = 7.0$  Hz, H-25);  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  220.6 (s, C-5), 170.3 (s, C-1), 161.0 (s, C-20), 138.6 (s, C-12), 138.4 (s, C-16), 137.5 (s, C-18), 135.6 (d, C-19), 120.8 (d, C-13), 115.8 (d, C-17), 78.9 (d, C-15), 74.3 (d, C-7), 72.7 (d, C-3), 53.3 (s, C-4), 42.0 (d, C-6), 39.6 (t, C-2), 38.6 (d, C-8), 32.4 (t, C-14), 31.9 (t, C-9), 31.6 (t, C-11), 25.6 (t, C-10), 23.0 (q, C-26), 22.8 (q, C-23), 18.8 (q, C-22), 16.1 (q, C-27), 15.9 (q, C-25), 13.8 (q, C-21), 13.6 (q, C-24); EIIMS  $m/z$  475 [M]<sup>+</sup> (11), 288 (9), 287 (5), 188 (7), 171 (32), 152 (100);

111 (10); HREIMS  $m/z$  475.2913 (calcd. for  $C_{27}H_{41}NO_6$ , 475.2934).

**Epothilone C<sub>1</sub> (16):** colorless amorphous solid;  $[\alpha]^{22}_D -114.0$  (*c* 10.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 211 (16500), 248 (12500); IR (KBr)  $\nu_{\text{max}}$  3440, 2933, 2877, 2858, 1730, 1708, 1457, 1244, 981  $\text{cm}^{-1}$ ; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  6.96 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.47 (1H, dd, *J* = 9.2, 3.0 Hz, H-15), 5.43 (1H, m, H-12), 5.40 (1H, m, H-13), 4.40 (1H, ddd, *J* = 6.2, 6.1, 6.1 Hz, H-3), 3.69 (1H, dd, *J* = 5.7, 3.6 Hz, H-7), 3.01 (1H, dq, *J* = 5.7, 6.9 Hz, H-6), 3.01 (1H, bs, 3-OH), 2.84 (1H, dq, *J* = 5.2, 7.0 Hz, H-4), 2.68 (3H, s, H-21), 2.66 (1H, ddd, *J* = 16.4, 9.2, 7.3 Hz, H-14a), 2.64 (1H, dd, *J* = 15.9, 7.1 Hz, H-2a), 2.54 (1H, dd, *J* = 15.9, 6.1 Hz, H-2b), 2.38 (1H, bd, *J* = 16.4 Hz, H-14b), 2.35 (1H, bs, 7-OH), 2.07 (3H, bs, H-27), 2.03 (2H, m, H-11), 1.62 (1H, m, H-10a), 1.53 (1H, m, H-8), 1.35 (1H, m, H-9a), 1.22 (1H, m, H-9b), 1.19 (3H, d, *J* = 6.9 Hz, H-24), 1.14 (3H, d, *J* = 6.9 Hz, H-23), 1.10 (1H, m, H-10b), 0.95 (3H, d, *J* = 6.9 Hz, H-25); <sup>13</sup>C NMR, see Table 1; EIIMS *m/z* 463 [M]<sup>+</sup> (5), 324 (8), 290 (8), 204 (7), 168 (100), 164 (15), 139 (36); HREIMS *m/z* 463.2381 (calcd. for C<sub>25</sub>H<sub>37</sub>NO<sub>3</sub>S, 463.2392).

Epothilone D<sub>1</sub> (17): colorless amorphous solid;  $[\alpha]^{22}_D -118.6$  (*c* 0.5, MeOH); UV (MeOH)  $\lambda_{max}$  nm ( $\epsilon$ ) 208 (18300), 249 (11900); IR (KBr)  $\nu_{max}$  3439, 2965, 2934, 2877, 1729, 1707, 1456, 1250, 980 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  6.98 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.51 (1H, dd, *J* = 9.5, 3.4 Hz, H-15), 5.16 (1H, dd, *J* = 8.0, 4.2 Hz, H-13), 4.42 (1H, ddd, *J* = 7.1, 6.3, 5.5 Hz, H-3), 3.70 (1H, dd, *J* = 6.5, 2.9 Hz, H-7), 3.07 (1H, dq, *J* = 6.5, 6.9 Hz, H-6), 2.95 (1H, dq, *J* = 4.7, 7.0 Hz, H-4), 2.71 (3H, s, H-21), 2.69 (1H, dd, *J* = 16.0, 6.3 Hz, H-2a), 2.64 (1H, m, H-14a), 2.59 (1H, dd, *J* = 16.0, 7.1 Hz, H-2b), 2.46 (1H, bs, 3-OH), 2.38 (1H, bd, *J* = 16.0 Hz, H-14b), 2.19 (1H, ddd, *J* = 13.3, 8.6, 5.7 Hz, H-11a), 2.10 (3H, d, *J* = 1.4 Hz, H-27), 2.02 (1H, bs, 7-OH), 1.91 (1H, ddd, *J* = 13.3, 6.0, 6.0 Hz, H-11b), 1.68 (1H, m, H-10a), 1.66 (3H, bs, H-26), 1.53 (1H, m, H-8), 1.37 (1H, m, H-9a), 1.26 (1H, m, H-9b), 1.24 (3H, d, *J* = 6.9 Hz, H-24), 1.19 (1H, m, H-10b), 1.14 (3H, d, *J* = 7.0, H-23), 0.99 (3H, d, *J* = 6.9 Hz, H-25); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  217.0 (s, C-5), 169.7 (s, C-1), 165.0 (s, C-20), 152.2 (s, C-18), 138.5 (s, C-12), 137.7 (s, C-16), 120.7 (d, C-13), 120.1 (d, C-17), 116.3 (d, C-19), 78.8 (d, C-15), 77.2 (d, C-7), 67.7 (d, C-3), 52.1 (d, C-4), 46.5 (d, C-6), 40.6 (t, C-2), 37.6 (d, C-8), 32.3 (t, C-14), 31.8 (t, C-11), 29.5(t, C-9), 25.5 (t, C-10), 23.1 (q, C-26), 19.2 (q, C-21), 15.5 (q, C-27), 16.6 (q, C-25), 14.5 (q, C-24), 9.7 (q, C-23); EIMS *m/z* 477 [M]<sup>+</sup> (13), 304 (19), 303 (31), 218 (40), 204 (41), 168 (100), 164 (45), 157 (25), 139 (18); HREIMS *m/z* 477.2544 (calcd. for C<sub>26</sub>H<sub>39</sub>NO<sub>5</sub>S, 477.2549).

Epothilone C<sub>2</sub> (18): colorless amorphous solid;  $[\alpha]^{22}_D -11.6$  (*c* 10.0, MeOH); UV (MeOH)  $\lambda_{max}$  nm ( $\epsilon$ ) 212 (15500), 249 (12100); IR (KBr)  $\nu_{max}$  3428, 2962, 2929, 2877, 2859, 1734, 1705, 1460, 1251, 982 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  6.99 (1H, s, H-19), 6.66 (1H,

bs, H-17), 5.55 (1H, ddd,  $J = 10.4, 9.2, 6.1$  Hz, H-12), 5.38 (1H, ddd,  $J = 10.4, 9.3, 6.2$  Hz, H-13), 5.22 (1H, dd,  $J = 8.8, 2.8$  Hz, H-15), 4.42 (1H, dddd,  $J = 9.4, 5.6, 4.2, 4.1$  Hz, H-3), 3.93 (1H, d,  $J = 5.6$  Hz, 3-OH), 3.86 (1H, m, H-7), 3.15 (1H, bs, 7-OH), 3.12 (1H, dq,  $J = 4.2, 7.0$  Hz, H-4), 3.00 (1H, dq,  $J = 6.9, 7.0$  Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dddd,  $J = 15.1, 9.3, 8.8, 0.8$  Hz, H-14a), 2.58 (1H, dd,  $J = 15.4, 9.4$  Hz, H-2a), 2.38 (1H, dd,  $J = 15.4, 4.1$  Hz, H-2b), 2.31 (1H, ddd,  $J = 15.1, 6.2, 2.8$  Hz, H-14b), 2.08 (3H, d,  $J = 1.3$  Hz, H-27), 2.15 (1H, m, H-11a), 2.04 (1H, m, H-11b), 1.71 (1H, m, H-8), 1.59 (1H, m, H-10a), 1.43 (1H, m, H-9a), 1.31 (1H, m, H-9b), 1.26 (3H, d,  $J = 7.0$  Hz, H-24), 1.15 (3H, d,  $J = 7.0$  Hz, H-23), 1.11 (1H, m, H-10b), 1.00 (3H, d,  $J = 6.9$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463 [M] $^+$  (7), 324 (7), 306 (8), 290 (17), 168 (100), 164 (14), 139 (27); HREIMS  $m/z$  463.2392 (calcd. for  $\text{C}_{22}\text{H}_{33}\text{NO}_5\text{S}$ , 463.2392).

Epothilone D<sub>2</sub> (19): colorless amorphous solid;  $[\alpha]^{25}_D -12.5$  ( $c 1.0$ , MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 210 (15400), 248 (11200); IR (KBr)  $\nu_{\text{max}}$  3436, 2965, 2930, 2877, 1732, 1705, 1458, 1253, 980  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  6.97 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.18 (1H, dd,  $J = 7.9, 4.9$  Hz, H-15), 5.18 (1H, ddd,  $J = 9.6, 5.4, 1.0$  Hz, H-13), 4.27 (1H, m, H-3), 3.88 (1H, dd,  $J = 5.6, 4.6$  Hz, H-7), 3.19 (1H, bs, 3-OH), 3.07 (1H, dq,  $J = 4.3, 7.0$  Hz, H-4), 2.95 (1H, dq,  $J = 5.6, 7.0$  Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dd,  $J = 14.9, 7.8$  Hz, H-2a), 2.56 (1H, ddd,  $J = 14.7, 9.6, 7.9$  Hz, H-14a), 2.43 (1H, dd,  $J = 14.9, 5.6$  Hz, H-2b), 2.38 (1H, bs, 7-OH), 2.26 (1H, ddd,  $J = 14.5, 5.4, 4.9$  Hz, H-14b), 2.19 (1H, ddd,  $J = 13.0, 10.4, 5.4$  Hz, H-11a), 2.10 (3H, d,  $J = 1.4$  Hz, H-27), 1.95 (1H, ddd,  $J = 13.0, 10.3, 5.3$  Hz, H-11b), 1.72 (1H, m, H-8), 1.68 (3H, bs, H-26), 1.61 (1H, m, H-10a), 1.39 (2H, m, H-9), 1.21 (1H, m, H-10b)

1.19 (3H, d,  $J = 6.9$  Hz, H-24), 1.17 (3H, d,  $J = 7.0$ , H-22), 1.00 (3H, d,  $J = 6.9$  Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  216.8 (s, C-5), 170.4 (s, C-1), 164.9 (s, C-20), 152.3 (s, C-18), 139.8 (s, C-12), 137.5 (s, C-16), 120.5 (d, C-17), 119.2 (d, C-13), 116.3 (d, C-19), 80.0 (d, C-15), 74.3 (d, C-7), 69.7 (d, C-3), 48.6 (d, C-4), 48.4 (d, C-6), 39.9 (t, C-2), 36.6 (d, C-8), 32.2 (t, C-14), 32.7 (t, C-11), 30.9 (t, C-9), 26.0 (t, C-10), 23.6 (q, C-26), 19.2 (q, C-21), 15.4 (q, C-27), 17.1 (q, C-25), 12.4 (q, C-24), 12.7 (q, C-23); EIIMS  $m/z$  477 [M] $^+$  (22), 304 (19), 303 (17), 218 (22), 204 (25), 168 (100), 164 (28), 157 (31), 139 (21); HREIMS  $m/z$  477.2545 (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_5\text{S}$ , 477.2549).

Epothilone C<sub>3</sub> (20): colorless amorphous solid;  $[\alpha]^{22}_D -62.1$  ( $c$  5.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 212 (16200), 248 (12300); IR (KBr)  $\nu_{\text{max}}$  3432, 2928, 2878, 2858, 1736, 1698, 1252, 1040  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.95 (1H, s, H-19), 6.56 (1H, bs, H-17), 5.44 (1H, ddd,  $J = 10.9, 10.3, 5.4$  Hz, H-12), 5.33 (1H, ddd,  $J = 10.9, 9.3, 4.6$  Hz, H-13), 5.23 (1H, dd,  $J = 9.5, 2.2$  Hz, H-15), 4.36 (1H, ddd,  $J = 11.3, 5.6, 2.3$  Hz, H-3), 4.04 (1H, d,  $J = 5.6$  Hz, 3-OH), 3.93 (1H, ddd,  $J = 9.5, 2.3, 1.4$  Hz, H-7), 3.56 (1H, bd,  $J = 2.3$  Hz, 7-OH), 2.70 (1H, dd,  $J = 18.0, 1.4$  Hz, H-6a), 2.67 (3H, s, H-21), 2.61 (1H, ddd,  $J = 15.3, 9.5, 9.3$  Hz, H-14a), 2.38 (1H, dd,  $J = 14.3, 11.3$  Hz, H-2a), 2.36 (1H, dd,  $J = 18.0, 9.5$  Hz, H-6b), 2.28 (1H, bd,  $J = 15.3$  Hz, H-14b), 2.12 (1H, m, H-11a), 2.06 (1H, dd,  $J = 14.3, 2.3$  Hz, H-2b), 2.03 (3H, d,  $J = 1.3$  Hz, H-27), 1.96 (1H, m, H-11b), 1.75 (1H, m, H-8), 1.54 (1H, m, H-10a), 1.26 (1H, m, H-9a), 1.25 (3H, s, H-23), 1.17 (1H, m, H-10b), 1.15 (1H, m, H-9b), 1.03 (3H, s, H-22), 0.91 (3H, d,  $J = 6.8$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIIMS  $m/z$  463 [M] $^+$  (28), 290 (14), 168 (100), 164 (36), 157 (44), 151 (25); HREIMS  $m/z$  463.2379 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

**Epothilone C<sub>4</sub> (21):** colorless amorphous solid;  $[\alpha]^{22}_{\text{D}} -75.6$  (*c* 1.0, MeOH); UV (MeOH)

$\lambda_{\text{max}}$  nm ( $\epsilon$ ) 212 (17200), 248 (12500); IR (KBr)  $\nu_{\text{max}}$  3434, 2974, 2932, 2859, 1735, 1686, 1252, 1046 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  6.96 (1H, s, H-19), 6.60 (1H, bs, H-17), 5.43 (1H, m, H-12), 5.40 (1H, m, H-13), 5.26 (1H, dd, *J* = 9.6, 2.3 Hz, H-15), 4.41 (1H, ddd, *J* = 11.4, 5.8, 2.5 Hz, H-3), 3.78 (1H, m, H-7), 3.70 (1H, bs, 3-OH), 3.46 (1H, d, *J* = 0.9 Hz, 7-OH), 3.01 (1H, dq, *J* = 0.5, 7.0 Hz, H-6), 2.69 (3H, s, H-21), 2.66 (1H, ddd, *J* = 15.3, 9.6, 8.8 Hz, H-14a), 2.47 (1H, dd, *J* = 14.5, 11.4 Hz, H-2a), 2.29 (1H, m, H-14b), 2.25 (1H, dd, *J* = 14.5, 2.5 Hz, H-2b), 2.24 (1H, m, H-11a), 2.07 (3H, d, *J* = 1.4 Hz, H-27), 1.96 (1H, m, H-11b), 1.51 (2H, m, H-8), 1.44 (2H, m, H-10), 1.37 (2H, m, H-9), 1.32 (3H, s, H-23), 1.17 (3H, d, *J* = 7.0 Hz, H-24), 1.07 (3H, s, H-22); <sup>13</sup>C NMR, see Table 1; EIIMS *m/z* 463 [M]<sup>+</sup> (7), 276 (15), 171 (33), 168 (100), 164 (23), 151 (22), 111 (13); HREIMS *m/z* 463.2373 (calcd. for C<sub>25</sub>H<sub>37</sub>NO<sub>5</sub>S, 463.2392).

**Epothilone C<sub>5</sub> (22):** colorless amorphous solid;  $[\alpha]^{22}_{\text{D}} -158.2$  (*c* 0.5, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 205 (19500), 247 (12700); IR (KBr)  $\nu_{\text{max}}$  3447, 2972, 2927, 1737, 1690, 1450, 1252, 1181, 986 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  6.93 (1H, s, H-19), 6.48 (1H, bs, H-17), 5.48 (1H, ddd, *J* = 10.7, 6.2, 6.2 Hz, H-12), 5.39 (1H, m, H-13), 5.37 (1H, m, H-9), 5.34 (1H, dd, *J* = 8.0, 2.3 Hz, H-15), 4.29 (1H, dd, *J* = 6.0, 2.6 Hz, H-7), 4.09 (1H, ddd, *J* = 10.8, 7.1, 2.9 Hz, H-3), 3.59 (1H, d, *J* = 7.1 Hz, 3-OH), 3.17 (1H, dq, *J* = 6.0, 6.9 Hz, H-6), 2.68 (3H, s, H-21), 2.54 (1H, ddd, *J* = 15.2, 8.1, 8.0 Hz, H-14a), 2.44 (1H, bs, 7-OH), 2.42 (1H, dd, *J* = 15.1, 2.9 Hz, H-2a), 2.41 (1H, ddd, *J* = 15.2, 2.3, 2.3 Hz, H-14b), 2.34 (1H, dd, *J* = 15.1, 10.8 Hz, H-2b), 2.20 (1H, m, H-10a), 2.18 (2H, m, H-11), 2.12 (1H, m, H-10b), 2.06 (3H, bs, H-27), 1.67 (3H, bs, H-25), 1.27 (3H, s, H-23), 1.21 (3H, d, *J* = 6.9 Hz, H-24), 1.15 (3H, s, H-22); <sup>13</sup>C NMR,

see Table 1; EIIMS  $m/z$  475 [M]<sup>+</sup> (6), 392 (7), 304 (6), 288 (33), 204 (76), 171 (19), 168 (100), 164 (12); HREIMS  $m/z$  475.2380 (calcd. for C<sub>26</sub>H<sub>31</sub>NO<sub>5</sub>S, 475.2392).

**Epothilone D<sub>5</sub>** (23): colorless amorphous solid;  $[\alpha]^{22}_D -150$  (*c* 0.2, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 205 (23300), 248 (13600); IR (KBr)  $\nu_{\text{max}}$  3439, 2967, 2927, 1736, 1690, 1451, 1254, 1181, 987 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$ : 6.94 (1H, s, H-19), 6.51 (1H, bs, H-17), 5.34 (1H, bs, H-9), 5.29 (1H, dd, *J* = 8.0, 2.4 Hz, H-15), 5.16 (1H, dd, *J* = 8.2, 6.2 Hz, H-13), 4.30 (1H, bd, *J* = 4.9 Hz, H-7), 4.19 (1H, ddd, *J* = 10.8, 7.6, 3.0 Hz, H-3), 3.68 (1H, d, *J* = 7.6 Hz, 3-OH), 3.17 (1H, dq, *J* = 4.9, 7.0 Hz, H-6), 2.69 (3H, s, H-21), 2.65 (1H, d, *J* = 2.1 Hz, 7-OH), 2.56 (1H, ddd, *J* = 16.2, 8.2, 8.0 Hz, H-14a), 2.40 (1H, dd, *J* = 15.0, 3.0 Hz, H-2a), 2.39 (1H, bd, *J* = 16.2 Hz, H-14b), 2.34 (1H, dd, *J* = 15.0, 10.8 Hz, H-2b), 2.25 (2H, m, H-10a and H-11a), 2.20 (1H, m, H-10b), 2.17 (1H, m, H-11b), 2.05 (3H, d, *J* = 1.0 Hz, H-27), 1.69 (3H, bs, H-25), 1.68 (3H, bs, H-26), 1.29 (3H, s, H-23), 1.23 (3H, d, *J* = 7.0 Hz, H-24), 1.16 (3H, s, H-22); <sup>13</sup>C NMR, see Table 1; EIIMS  $m/z$  489 [M]<sup>+</sup> (4), 406 (4), 338 (7), 302 (13), 218 (35), 171 (10), 168 (100), 153 (20), 125 (10); HREIMS  $m/z$  489.2536 (calcd. for C<sub>27</sub>H<sub>31</sub>NO<sub>5</sub>S, 489.2549).

**Epothilone C<sub>6</sub>** (24): colorless amorphous solid;  $[\alpha]^{22}_D -205.2$  (*c* 1.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 218 (24600), 237 (28800); IR (KBr)  $\nu_{\text{max}}$  3435, 2967, 2927, 2882, 1732, 1688, 1465, 1258, 988 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  6.97 (1H, s, H-19), 6.58 (1H, bs, H-17), 6.43 (1H, dd, 15.5, 10.8 Hz, H-11), 6.11 (1H, dd, *J* = 10.8, 10.6 Hz, H-12), 5.75 (1H, ddd, *J* = 15.5, 8.3, 5.6 Hz, H-10), 5.34 (1H, m, H-13), 5.34 (1H, dd, *J* = 9.7, 2.4 Hz, H-15), 4.16 (1H, ddd, *J* = 9.2, 4.9, 4.3 Hz, H-3), 3.74 (1H, ddd, *J* = 2.2, 2.1, 1.7 Hz, H-7), 3.24 (1H, dq, *J* = 2.1, 6.9 Hz, H-6), 3.06 (1H, d, *J* = 2.2 Hz, 7-OH), 2.93 (1H, d, *J* = 4.9 Hz, 3-OH), 2.78 (1H, dddd,

$J = 14.1, 9.9$ , 9.7, 0.7, H-14a), 2.71 (3H, s, H-21), 2.48 (1H, m, H-9a), 2.47 (1H, dd,  $J = 15.5$ , 9.2 Hz, H-2a), 2.40 (1H, dd,  $J = 15.5$ , 4.3 Hz, H-2b), 2.38 (1H, bdd,  $J = 14.1$ , 7.8 Hz, H-14b), 2.11 (3H, d,  $J = 1.3$  Hz, H-27), 1.96 (1H, m, H-8), 1.33 (3H, s, H-23), 1.11 (3H, d,  $J = 6.9$  Hz, H-24), 1.06 (3H, s, H-22), 1.05 (3H, d,  $J = 6.8$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  475 [M]<sup>+</sup> (13), 387 (2), 316 (4), 288 (15), 230 (16), 204 (9), 171 (18), 168 (100), 164 (14), 151 (17); HREIMS  $m/z$  475.2361 (calcd. for  $\text{C}_{26}\text{H}_{37}\text{NO}_5\text{S}$ , 475.2392).

Epothilone C<sub>7</sub> (25): colorless amorphous solid;  $[\alpha]_D^{22} -XXX$  (*c* 2.0, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) XXX (XXX), XXX (XXX); IR (KBr)  $\nu_{\max}$  XXX cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.01 (1H, s, H-19), 6.66 (1H, bs, H-17), 5.59 (1H, ddd,  $J = 11.1$ , 11.1, 3.8 Hz, H-12), 5.40 (1H, dd,  $J = 11.1$ , 9.2, H-13), 5.03 (1H, d,  $J = 9.3$  Hz, H-15), 4.62 (1H, dd,  $J = 9.3$ , 9.2 Hz, H-14), 4.18 (1H, bd,  $J = 11.0$  Hz, H-3), 3.72 (1H, bs, H-7), 3.20 (1H, bs, 3-OH), 3.09 (1H, dq,  $J = 1.9$ , 6.8 Hz, H-6), 3.00 (1H, bs, 7-OH), 2.69 (3H, s, H-21), 2.47 (1H, dd,  $J = 14.8$ , 11.0 Hz, H-2a), 2.32 (1H, dd,  $J = 14.8$ , 2.6 Hz, H-2b), 2.27 (1H, m, H-11a), 2.19 (3H, bs, H-27), 2.13 (1H, m, H-11b), 1.76 (1H, m, H-8), 1.70 (1H, m, H-10a), 1.35 (1H, m, H-9a), 1.32 (3H, s, H-23), 1.23 (1H, m, H-9b), 1.21 (1H, m, H-10b), 1.18 (3H, d,  $J = 6.8$  Hz, H-24), 1.08 (3H, s, H-22), 1.00 (3H, d,  $J = 6.9$  Hz, H-25); EIMS  $m/z$  493 [M]<sup>+</sup> XXX; HREIMS  $m/z$  493.XXX (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_6\text{S}$ , 493.2498).

Epothilone C<sub>8</sub> (26): colorless amorphous solid;  $[\alpha]_D^{22} -75.2$  (*c* 2.5, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 210 (16800), 248 (17800); IR (KBr)  $\nu_{\max}$  3443, 2932, 2881, 1734, 1689, 1465, 1255, 1183, 976 cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  6.93 (1H, s, H-19), 6.62 (1H, dd,  $J = 15.6$ , 0.6 Hz, H-17), 6.49 (1H, dd,  $J = 15.6$ , 6.6 Hz, H-16), 5.52 (1H, dddd,  $J = 9.5$ , 6.6, 2.8, 0.6 Hz, H-

15), 5.42 (1H, m, H-12), 5.41 (1H, m, H-13), 4.13 (1H, ddd,  $J = 11.0, 5.3, 2.8$  Hz, H-3), 3.69 (1H, ddd,  $J = 3.7, 2.8, 2.5$  Hz, H-7), 3.11 (1H, dq,  $J = 2.5, 6.8$  Hz, H-6), 2.95 (1H, d,  $J = 5.3$  Hz, 3-OH), 2.90 (1H, d,  $J = 2.8$  Hz, 7-OH), 2.69 (3H, s, H-21), 2.67 (1H, ddd,  $J = 14.9, 9.5, 8.4$  Hz, H-14a), 2.48 (1H, dd,  $J = 15.6, 11.0$  Hz, H-2a), 2.33 (1H, dd,  $J = 15.6, 2.8$  Hz, H-2b), 2.30 (1H, bd,  $J = 14.9$  Hz, H-14b), 2.14 (1H, m, H-11a), 2.03 (1H, m, H-11b), 1.71 (1H, m, H-8), 1.63 (1H, m, H-10a), 1.31 (1H, m, H-9a), 1.29 (3H, s, H-23), 1.17 (3H, d,  $J = 6.8$  Hz, H-24), 1.16 (1H, m, H-10b), 1.14 (1H, m, H-9b), 1.05 (3H, s, H-22), 0.97 (3H, d,  $J = 7.1$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463 [M]<sup>+</sup> (21), 310 (10), 276 (21), 171 (83), 154 (100), 150 (27), 111 (18); HREIMS  $m/z$  463.2382 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

Epothilone C<sub>9</sub> (27): colorless amorphous solid;  $[\alpha]^{25}_{\text{D}} -93.4$  ( $c$  1.0, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 209 (15200), 254 (15700); IR (KBr)  $\nu_{\text{max}}$  3416, 2966, 2932, 1736, 1689, 1463, 1249, 1011 cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  7.06 (1H, s, H-19), 6.65 (1H, bs, H-17), 6.56 (1H, dd,  $J = 10.6, 4.4$  Hz, 27-OH), 5.55 (1H, d,  $J = 6.2$  Hz, 3-OH), 5.52 (1H, dd,  $J = 11.6, 2.0$  Hz, H-15), 5.44 (1H, dddd,  $J = 11.2, 10.7, 3.1, 1.7$  Hz, H-12), 5.35 (1H, dddd,  $J = 11.0, 10.7, 3.9, 1.7$  Hz, H-13), 4.47 (1H, ddd,  $J = 12.5, 4.4, 1.3$  Hz, H-27a), 4.35 (1H, ddd,  $J = 11.7, 6.2, 2.6$  Hz, H-3), 4.20 (1H, ddd,  $J = 12.5, 10.6, 0.9$  Hz, H-27b), 3.63 (1H, ddd,  $J = 4.6, 1.8, 0.9$  Hz, H-7), 3.24 (1H, d,  $J = 1.8$  Hz, 7-OH), 3.13 (1H, dq,  $J = 0.9, 6.8$  Hz, H-6), 2.80 (1H, ddd,  $J = 14.8, 11.6$ , 11.0 Hz, H-14a), 2.71 (3H, s, H-21), 2.40 (1H, dd,  $J = 14.4, 11.7$  Hz, H-2a), 2.24 (1H, m, H-11a), 2.06 (1H, dd,  $J = 14.4, 2.6$  Hz, H-2b), 2.01 (1H, ddd,  $J = 14.8, 3.9, 2.0$  Hz, H-14b), 2.00 (1H, m, H-11b), 1.77 (1H, m, H-8), 1.69 (1H, m, H-10a), 1.35 (1H, m, H-9a), 1.35 (3H, s, H-23), 1.19 (1H, m, H-10b), 1.19 (3H, d,  $J = 6.8$  Hz, H-24), 1.18 (1H, m, H-9b), 1.01 (3H, d,  $J =$

7.1 Hz, H-25), 0.98 (3H, s, H-22);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  493 [M]<sup>+</sup> (17), 306 (64), 184 (50), 171 (30), 167 (38), 166 (100), 138 (12); HREIMS  $m/z$  493.2502 (calcd. for  $\text{C}_{26}\text{H}_{39}\text{NO}_6\text{S}$ , 493.2498).

**trans-Epothilone C<sub>1</sub>** (28): colorless amorphous solid;  $[\alpha]^{22}_{\text{D}} -84$  (*c* 0.2, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 21.1 (17400), 248 (12900); IR (KBr)  $\nu_{\text{max}}$  3433, 2961, 2933, 2879, 1730, 1708, 1457, 1251, 975  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$  7.00 (1H, s, H-19), 6.64 (1H, bs, H-17), 5.45 (1H, ddd, *J* = 15.2, 6.5, 6.5 Hz, H-12), 5.42 (1H, dd, *J* = 6.4, 3.7 Hz, H-15), 5.35 (1H, dt, *J* = 15.2, 7.1 Hz, H-13), 4.42 (1H, m, H-3), 3.58 (1H, ddd, *J* = 8.1, 7.9, 2.8 Hz, H-7), 3.24 (1H, m, H-6), 3.14 (1H, dq, *J* = 4.0, 6.9 Hz, H-6), 2.92 (1H, d, *J* = 7.9 Hz, 7-OH), 2.71 (3H, s, H-21), 2.71 (2H, m, H-2), 2.53 (2H, m, H-14), 2.17 (1H, d, *J* = 2.17 Hz, 3-OH), 2.11 (1H, m, H-11a), 2.06 (3H, bs, H-27), 1.93 (1H, m, H-11b), 1.68 (1H, m, H-9a), 1.65 (1H, m, H-10a), 1.33 (1H, m, H-8), 1.26 (3H, d, *J* = 6.8 Hz, H-24), 1.16 (1H, m, H-10b), 1.12 (3H, d, *J* = 6.9 Hz, H-22), 1.07 (1H, m, H-9b), 1.00 (3H, d, *J* = 6.8 Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463 [M]<sup>+</sup> (6), 290 (21), 289 (20), 204 (23), 194 (19), 190 (22), 168 (100), 164 (48), 157 (14), 152 (19), 151 (17), 139 (15), 111 (18); HREIMS  $m/z$  463.2371 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

**trans-Epothilone C<sub>2</sub>** (29): colorless amorphous solid;  $[\alpha]^{22}_{\text{D}} -3$  (*c* 1.5, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 211 (15800), 248 (11900); IR (KBr)  $\nu_{\text{max}}$  3435, 2963, 2931, 2878, 1731, 1706, 1457, 1273, 979  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 600 MHz)  $\delta$  6.99 (1H, s, H-19), 6.57 (1H, bs, H-17), 5.56 (1H, ddd, *J* = 15.1, 7.4, 7.0 Hz, H-12), 5.41 (1H, ddd, *J* = 15.1, 7.0, 6.9 Hz, H-13), 5.41 (1H, dd, *J* = 7.7, 2.8 Hz, H-15), 4.13 (1H, dddd, *J* = 6.7, 6.2, 5.6, 5.1 Hz, H-3), 3.78 (1H, ddd, *J* = 8.2, 6.5, 1.9 Hz, H-7), 3.18 (1H, d, *J* = 5.6 Hz, 3-OH), 3.06 (1H, dq, *J* = 8.2, 7.1 Hz,

H-6), 2.98 (1H, dq,  $J = 6.2, 7.0$  Hz, H-4), 2.71 (3H, s, H-21), 2.64 (1H, dd,  $J = 15.1, 6.7$  Hz, H-2a), 2.54 (1H, dd,  $J = 15.1, 5.1$  Hz, H-2b), 2.44 (2H, m, H-14), 2.22 (1H, dddd,  $J = 13.8, 7.0, 6.2, 2.9$  Hz, H-11a), 2.10 (3H, d,  $J = 1.1$  Hz, H-27), 2.09 (1H, d,  $J = 6.5$  Hz, 7-OH), 1.88 (1H, dddd,  $J = 13.8, 10.9, 7.4, 2.9$  Hz, H-11b), 1.65 (1H, m, H-8), 1.63 (1H, m, H-10a), 1.56 (1H, dddd,  $J = 12.7, 12.7, 3.9, 3.9$  Hz, H-9a), 1.20 (3H, d,  $J = 7.1$  Hz, H-24), 1.15 (3H, d,  $J = 7.0$  Hz, H-23), 1.13 (1H, m, H-10b), 1.04 (1H, m, H-9b), 1.01 (3H, d,  $J = 7.0$  Hz, H-25);  $^{13}\text{C}$  NMR, see Table 1; EIMS  $m/z$  463 [M]<sup>+</sup> (13), 290 (11), 190 (10), 168 (100), 164 (20), 157 (26), 139 (17); HREIMS  $m/z$  463.2383 (calcd. for  $\text{C}_{25}\text{H}_{37}\text{NO}_5\text{S}$ , 463.2392).

**Epothilone I<sub>1</sub>** (30): colorless amorphous solid;  $[\alpha]_D^{25} -XXX$  (*c* XXX, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) XXX; IR (KBr)  $\nu_{\text{max}}$  XXX cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  6.96 (1H, s, H-19), 6.54 (1H, bs, H-17), 5.49 (1H, ddd,  $J = 10.3, 7.3, 7.3$  Hz, H-12), 5.33 (1H, dd,  $J = 8.3, 4.4$  Hz, H-15), 5.31 (1H, m, H-13), 4.15 (1H, ddd,  $J = 8.0, 5.0, 4.6$  Hz, H-3), 3.80 (1H, m, H-7), 3.21 (1H, dq,  $J = 6.0, 6.9$  Hz, H-6), 2.89 (1H, d,  $J = 5.0$  Hz, 3-OH); 2.70 (3H, s, H-21), 2.65 (1H, ddd,  $J = 15.8, 8.5, 8.3$  Hz, H-14a), 2.42 (2H, m, H-2), 2.35 (1H, m, H-14b), 2.27 (1H, bd,  $J = 3.3$  Hz, 7-OH), 2.13 (1H, m, H-11a), 2.09 (3H, d,  $J = 1.2$  Hz, H-27), 2.00 (1H, m, H-11b), 1.72 (1H, m, H-8), 1.40 (2H, m, H-10<sub>b</sub>), 1.37 (1H, m, H-9<sub>p</sub>a), 1.36 (2H, m, H-9<sub>a</sub>), 1.32 (3H, s, H-23), 1.27 (3H, m, H-9<sub>p</sub>b and H-10<sub>a</sub>), 1.13 (3H, d,  $J = 6.9$  Hz, H-24), 1.09 (3H, s, H-22), 0.94 (3H, d,  $J = 6.9$  Hz, H-25);  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 75 MHz)  $\delta$  221.3 (s, C-5), 171.1 (s, C-1), 164.8 (s, C-20), 152.4 (s, C-18), 137.4 (s, C-16), 133.8 (d, C-12), 124.6 (d, C-13), 120.0 (d, C-17), 116.2 (d, C-19), 78.8 (d, C-15), 74.9 (d, C-7), 74.7 (d, C-3), 51.6 (s, C-4), 43.7 (d, C-6), 38.9 (t, C-2), 34.3 (d, C-8), 31.6 (t, C-14), 29.3 (t, C-9<sub>a</sub>), 28.6 (t, C-10<sub>p</sub>), 28.2 (t, C-10<sub>a</sub>), 26.6 (t, C-

11), 24.8 (t, C-9<sub>b</sub>), 23.6 (q, C-22), 19.3 (q, C23), 19.3 (q, C-21), 16.5 (q, C-25), 15.5 (q, C-27), 13.7 (q, C-24); EIMS *m/z* 505 [M]<sup>+</sup> XXX; HREIMS *m/z* 505.XXX (calcd. for C<sub>28</sub>H<sub>43</sub>NO<sub>5</sub>S, 505.XXX).

Epothilone I<sub>2</sub> (31): colorless amorphous solid;  $[\alpha]_D^{22}$  -XXX (*c* XXX, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm (*ε*) XXX; IR (KBr)  $\nu_{\text{max}}$  XXX cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz) δ 6.95 (1H, s, H-19), 6.53 (1H, bs, H-17), 5.40 (1H, m, H-12), 5.38 (1H, dd, *J* = 9.8, 3.3 Hz, H-15), 5.37 (1H, m, H-13), 4.21 (1H, ddd, *J* = 8.6, 3.8, 3.6 Hz, H-3), 3.85 (1H, ddd, *J* = 8.5, 5.8, 2.2 Hz, H-7), 3.18 (1H, dq, *J* = 8.5, 7.0 Hz, H-6), 2.70 (3H, s, H-21), 2.65 (1H, ddd, *J* = 15.2, 9.8, 9.0 Hz, H-14a), 2.51 (1H, d, *J* = 3.6 Hz, 3-OH), 2.37 (2H, m, H-2), 2.32 (1H, bd, *J* = 15.2 Hz, H-14b), 2.09 (3H, d, *J* = 1.3 Hz, H-27), 2.07 (2H, m, H-11), 1.78 (1H, m, H-8), 1.65 (1H, d, *J* = 5.8 Hz, 7-OH), 1.57 (1H, m, H-10<sub>b</sub>a), 1.44 (1H, m, H-10<sub>a</sub>a), 1.42 (1H, m, H-9<sub>b</sub>), 1.32 (3H, s, H-23), 1.21 (1H, m, H-10<sub>b</sub>b), 1.17 (3H, d, *J* = 7.0 Hz, H-24), 1.13 (2H, m, H-9<sub>a</sub>), 1.06 (3H, s, H-22), 0.95 (3H, d, *J* = 7.0 Hz, H-25<sub>a</sub>), 0.91 (3H, d, *J* = 6.5 Hz, H-25<sub>b</sub>), 0.68 (1H, m, H-10<sub>a</sub>b); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ 220.4 (s, C-5), 171.3 (s, C-1), XXX (s, C-20), 152.4 (s, C-18), 137.6 (s, C-16), 134.5 (d, C-12), 125.3 (d, C-13), 119.6 (d, C-17), 116.2 (d, C-19), 78.6 (d, C-15), 77.2 (d, C-7), 75.0 (d, C-3), 51.0 (s, C-4), 44.6 (d, C-6), 38.2 (t, C-2), 36.9 (t, C-9<sub>a</sub>), 34.5 (t, C-10<sub>a</sub>), 32.6 (d, C-8), 32.0 (t, C-14), 30.0 (d, C-9<sub>b</sub>), 27.4 (t, C-11), 26.6 (t, C-10<sub>b</sub>), 25.0 (q, C-22), 21.5 (q, C-25<sub>b</sub>), 19.3 (q, C-21), 17.9 (q, C-25<sub>a</sub>), 17.7 (q, C-23), 15.8 (q, C-24), 15.6 (q, C-27); EIMS *m/z* 519 [M]<sup>+</sup> XXX; HREIMS *m/z* 519.XXX (calcd. for C<sub>29</sub>H<sub>45</sub>NO<sub>5</sub>S, 519.XXX).

Epothilone I<sub>3</sub> (32): colorless amorphous solid;  $[\alpha]_D^{22}$  -XXX (*c* XXX, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm (*ε*) XXX; IR (KBr)  $\nu_{\text{max}}$  XXX cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz) δ 6.95 (1H,

s, H-19), 6.52 (1H, bs, H-17), 5.32 (1H, dd,  $J = 9.1, 3.0$  Hz, H-15), 5.08 (1H, dd,  $J = 8.5, 3.9$  Hz, H-13), 4.13 (1H, ddd,  $J = 9.4, 4.3, 3.2$  Hz, H-3), 3.81 (1H, m, H-7), 3.18 (1H, dq,  $J = 6.8,$  7.0 Hz, H-6), 2.83 (1H, d,  $J = 4.3$  Hz, 3-OH), 2.70 (3H, s, H-21), 2.61 (1H, ddd,  $J = 15.8, 9.1,$  8.5 Hz, H-14a), 2.43 (1H, dd,  $J = 14.0, 3.2$  Hz, H-2a), 2.38 (2H, dd,  $J = 14.0, 9.4$  Hz, H-2b), 2.30 (1H, bd,  $J = 15.8$  Hz, H-14b), 2.16 (1H, ddd,  $J = 14.1, 8.3, 7.4$  Hz, H-11a), 2.08 (3H, d,  $J = 1.0$  Hz, H-27), 1.99 (1H, d,  $J = 4.7$  Hz, 7-OH), 1.92 (1H, ddd,  $J = 14.1, 6.3, 6.3$  Hz, H-11b), 1.82 (1H, m, H-8), 1.67 (3H, s, H-26), 1.51 (1H, m, H-10<sub>β</sub>a), 1.40 (1H, m, H-9<sub>β</sub>b), 1.33 (1H, m, H-10<sub>β</sub>b), 1.31 (3H, s, H-23), 1.27 (1H, m, H-10<sub>α</sub>a), 1.23 (1H, m, H-9<sub>α</sub>a), 1.16 (3H, d,  $J = 7.0$  Hz, H-24), 1.10 (1H, m, H-9<sub>α</sub>b), 1.07 (3H, s, H-22), 0.95 (3H, d,  $J = 7.0$  Hz, H-25<sub>α</sub>), 0.92 (3H, d,  $J = 6.5$  Hz, H-25<sub>β</sub>), 0.75 (1H, m, H-10<sub>α</sub>b); EIMS  $m/z$  533 [M]<sup>+</sup> XXX; HREIMS  $m/z$  533.XXX (calcd. for C<sub>30</sub>H<sub>47</sub>NO<sub>5</sub>S, 533.XXX).

Epothilone I<sub>4</sub> (33): colorless amorphous solid;  $[\alpha]_{D}^{22} -XXX$  (*c* XXX, MeOH); UV (MeOH)  $\lambda_{max}$  nm ( $\epsilon$ ) XXX; IR (KBr)  $\nu_{max}$  XXX cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  6.95 (1H, s, H-19), 6.53 (1H, bs, H-17), 5.47 (1H, dt,  $J = 11.1, 5.8$  Hz, H-12), 5.33 (1H, ddd,  $J = 9.2, 3.9,$  0.5 Hz, H-15), 5.33 (1H, m, H-13), 4.09 (1H, dddd,  $J = 9.6, 8.1, 4.5, 3.3$  Hz, H-3), 3.83 (1H, m, H-7), 3.57 (1H, bs, 3-OH), 2.89 (1H, dq,  $J = 7.4, 7.1$  Hz, H-6), 2.83 (1H, dq,  $J = 8.1, 7.1$  Hz, H-4), 2.70 (3H, s, H-21), 2.64 (1H, m, H-14a), 2.42 (1H, dd,  $J = 14.2, 3.3$  Hz, H-2a), 2.43 (1H, dd,  $J = 14.2, 9.6$  Hz, H-2b), 2.30 (1H, m, H-14b), 2.10 (3H, d,  $J = 1.3$  Hz, H-27), 2.09 (2H, m, H-11), 1.81 (1H, m, H-8), 1.74 (1H, bd,  $J = 5.6$  Hz, 7-OH), 1.53 (1H, m, H-10<sub>β</sub>a), 1.49 (1H, m, H-9<sub>β</sub>b), 1.47 (1H, m, H-10<sub>α</sub>a), 1.27 (1H, m, H-10<sub>β</sub>b), 1.24 (1H, m, H-9<sub>α</sub>a), 1.17 (3H, d,  $J = 7.1$  Hz, H-23), 1.14 (1H, m, H-9<sub>α</sub>b), 1.08 (3H, d,  $J = 7.1$  Hz, H-24), 0.97 (3H, d,  $J = 6.9$  Hz, H-25<sub>α</sub>).

0.91 (3H, d,  $J = 6.5$  Hz, H-25 $\beta$ ), 0.79 (1H, m, H-10 $\alpha$ b);  $^{13}\text{C}$  NMR (CDCl<sub>3</sub>, 100 MHz)  $\delta$  217.0 (s, C-5), 170.8 (s, C-1), 164.8 (s, C-20), 152.4 (s, C-18), 137.1 (s, C-16), 134.6 (d, C-12), 124.7 (d, C-13), 120.2 (d, C-17), 116.4 (d, C-19), 78.7 (d, C-15), 76.4 (d, C-7), 71.3 (d, C-3), 50.7 (d, C-4), 50.1 (d, C-6), 40.7 (t, C-2), 38.5 (t, C-9 $\alpha$ ), 35.5 (t, C-10 $\alpha$ ), 33.4 (d, C-8), 31.8 (t, C-14), 30.0 (d, C-9 $\beta$ ), 27.2 (t, C-11), 26.7 (t, C-10 $\beta$ ), 21.4 (q, C-25 $\beta$ ), 19.3 (q, C-21), 18.2 (q, C-25 $\alpha$ ), 15.4 (q, C-27), 14.4 (q, C-24), 13.1 (q, C-23); EIMS  $m/z$  505 [M]<sup>+</sup> XXX; HREIMS  $m/z$  505.XXX (calcd. for C<sub>28</sub>H<sub>43</sub>NO<sub>5</sub>S, 505.XXX).

Epothilone I<sub>5</sub> (34): colorless amorphous solid;  $[\alpha]_D^{25} -XXX$  ( $c$  XXX, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) XXX; IR (KBr)  $\nu_{\text{max}}$  XXX cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  6.97 (1H, s, H-19), 6.52 (1H, bs, H-17), 5.32 (1H, dd,  $J = 7.1, 6.2$  Hz, H-15), 5.03 (1H, dd,  $J = 8.4, 5.0$  Hz, H-13), 4.05 (1H, dddd,  $J = 7.5, 7.2, 5.9, 4.6$  Hz, H-3), 3.91 (1H, m, H-7), 3.17 (1H, d,  $J = 5.9$  Hz, 3-OH), 2.94 (1H, dq,  $J = 7.2, 7.1$  Hz, H-4), 2.87 (1H, dq,  $J = 6.5, 6.9$  Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, dd,  $J = 14.6, 4.6$  Hz, H-2a), 2.60 (1H, m, H-14a), 2.53 (1H, dd,  $J = 14.6, 7.5$  Hz, H-2b), 2.31 (1H, m, H-14b), 2.10 (3H, d,  $J = 1.1$  Hz, H-27), 2.10 (1H, m, H-11a), 2.02 (1H, m, H-11b), 1.97 (1H, bd,  $J = 5.6$  Hz, 7-OH), 1.84 (1H, m, H-8), 1.66 (3H, s, H-26), 1.55 (1H, m, H-9 $\beta$ ), 1.49 (1H, m, H-10 $\beta$ a), 1.39 (1H, m, H-10 $\beta$ b), 1.33 (1H, m, H-10 $\alpha$ a), 1.31 (1H, m, H-9 $\alpha$ a), 1.15 (3H, d,  $J = 7.1$  Hz, H-23), 1.12 (1H, m, H-9 $\alpha$ b), 1.11 (3H, d,  $J = 6.9$  Hz, H-24), 0.97 (3H, d,  $J = 6.9$  Hz, H-25 $\alpha$ ), 0.94 (1H, m, H-10 $\alpha$ b), 0.93 (3H, d,  $J = 6.6$  Hz, H-25 $\beta$ ); EIMS  $m/z$  519 [M]<sup>+</sup> XXX; HREIMS  $m/z$  519.XXX (calcd. for C<sub>29</sub>H<sub>45</sub>NO<sub>5</sub>S, 519.XXX).

Epothilone I<sub>6</sub> (35): colorless amorphous solid;  $[\alpha]_D^{25} -XXX$  ( $c$  XXX, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) XXX; IR (KBr)  $\nu_{\text{max}}$  XXX cm<sup>-1</sup>;  $^1\text{H}$  NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  6.97 (1H,

s, H-19), 6.52 (1H, bs, H-17), 5.24 (1H, dd,  $J = 6.9, 6.9$  Hz, H-15), 5.02 (1H, dd,  $J = 8.8, 5.2$  Hz, H-13), 4.22 (1H, tdd,  $J = 6.1, 5.6, 4.8$  Hz, H-3), 3.76 (1H, ddd,  $J = 6.1, 5.7, 5.6$  Hz, H-7), 3.13 (1H, d,  $J = 5.6$  Hz, 3-OH), 3.05 (1H, dq,  $J = 4.8, 7.0$  Hz, H-4), 2.79 (1H, dq,  $J = 5.6, 6.9$  Hz, H-6), 2.70 (3H, s, H-21), 2.62 (1H, m, H-14a), 2.57 (2H, d,  $J = 6.1$  Hz, H-2a), 2.30 (1H, m, H-14b), 2.08 (3H, d,  $J = 1.0$  Hz, H-27), 2.02 (2H, m, H-11), 1.73 (1H, d,  $J = 6.1$  Hz, 7-OH), 1.69 (1H, m, H-8), 1.66 (3H, s, H-26), XXX (H-9<sub>a</sub>, H-9<sub>b</sub>, H-10<sub>a</sub>, H-10<sub>b</sub>), 1.21 (3H, d,  $J = 7.0$  Hz, H-22), 1.16 (3H, d,  $J = 6.9$  Hz, H-24), 0.94 (3H, d,  $J = 6.9$  Hz, H-25<sub>a</sub>), 0.91 (3H, d,  $J = 6.4$  Hz, H-25<sub>b</sub>); EIMS  $m/z$  519 [M]<sup>+</sup> XXX; HREIMS  $m/z$  519.XXX (calcd. for C<sub>29</sub>H<sub>45</sub>NO<sub>5</sub>S, 519.XXX).

Epothilone K (36): colorless amorphous solid;  $[\alpha]^{22}_D -7$  ( $c$  0.08, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ ) 212 (16700), 248 (12500); IR (KBr)  $\nu_{\max}$  3431, 2963, 2927, 2856, 1731, 1712, 1262, 1093, 1021, 802 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz)  $\delta$  6.95 (1H, s, H-19), 6.51 (1H, bs, H-17), 5.49 (3H, m, H-15, H-13, and H-12), 4.04 (1H, dddd,  $J = 7.9, 7.6, 6.9, 3.3$  Hz, H-3), 3.36 (1H, dq,  $J = 6.9, 6.8$  Hz, H-6), 2.83 (1H, d,  $J = 7.6$  Hz, 3-OH), 2.75 (1H, ddd,  $J = 16.1, 6.6, 3.4$  Hz, H-14a), 2.74 (1H, dd,  $J = 15.3, 3.3$  Hz, H-2a), 2.71 (3H, s, H-21), 2.58 (2H, m, H-14b and H-8), 2.50 (1H, dd,  $J = 15.3, 7.9$  Hz, H-2b), 2.29 (1H, m, H-11a), 2.10 (1H, m, H-11b), 2.09 (3H, d,  $J = 0.7$  Hz, H-27), 1.78 (1H, m, H-9a), 1.65 (1H, m, H-10a), 1.48 (1H, m, H-10b), 1.18 (1H, m, H-9b), 1.15 (3H, d,  $J = 6.8$  Hz, H-22), 1.03 (3H, d,  $J = 6.5$  Hz, H-25); EIMS  $m/z$  405 [M]<sup>+</sup> (38), 317 (12), 260 (9), 232 (10), 204 (14), 190 (16), 168 (100), 164 (30), 151 (28); HREIMS  $m/z$  405.XXX (calcd. for C<sub>26</sub>H<sub>39</sub>NO<sub>5</sub>S, 405.XXX).

(37): colorless amorphous solid;  $[\alpha]^{22}_D -27.5$  ( $c$  0.4, MeOH); UV (MeOH)  $\lambda_{\max}$  nm ( $\epsilon$ )

211 (16100), 247 (12100); IR (KBr)  $\nu_{\text{max}}$  3431, 2967, 2929, 2875, 1704, 1462, 1381, 1010  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.94 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.56 (1H, dtt,  $J$  = 10.8, 7.3, 1.4 Hz, H-12), 5.39 (1H, dtt,  $J$  = 10.8, 7.3, 1.4 Hz, H-13), 4.17 (1H, t,  $J$  = 6.6 Hz, H-15), 3.50 (1H, ddd,  $J$  = 8.7, 2.6, 2.6 Hz, H-7), 3.10 (1H, d,  $J$  = 2.6, 7-OH), 2.90 (1H, dq,  $J$  = 2.6, 7.2 Hz, H-6), 2.77 (1H, sep,  $J$  = 6.9 Hz, H-4), 2.70 (3H, s, H-21), 2.40 (2H, m, H-14), 2.07 (2H, m, H-11), 2.04 (3H, d,  $J$  = 1.1 Hz, H-27), 1.78 (1H, bs, 15-OH), 1.74 (1H, m, H-9a), 1.50 (1H, m, H-8), 1.46 (1H, m, H-10a), 1.27 (1H, m, H-10b), 1.11 (1H, m, H-9b), 1.094 (3H, d,  $J$  = 6.9 Hz, H-23), 1.089 (3H, d,  $J$  = 6.9 Hz, H-22), 1.08 (3H, d,  $J$  = 7.2 Hz, H-24), 0.82 (3H, d,  $J$  = 6.7 Hz, H-25);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  220.5 (s, C-5), 164.6 (s, C-20), 152.9 (s, C-18), 141.5 (s, C-16), 133.4 (d, C-12), 125.0 (d, C-13), 119.2 (d, C-17), 115.6 (d, C-19), 77.2 (d, C-15), 74.9 (d, C-7), 44.9 (d, C-6), 40.0 (d, C-4), 35.5 (d, C-8), 33.5 (t, C-14), 32.3 (t, C-9), 27.9 (t, C-11), 26.9 (t, C-10), 19.2 (q, C-21), 18.6 (q, C-23), 18.1 (q, C-22), 15.6 (q, C-25), 14.4 (q, C-27), 9.3 (q, C-24); EIIMS  $m/z$  407 [M]<sup>+</sup> (0.1), 204 (0.8), 168 (100), 140 (3.4); HREIMS  $m/z$  407.XXX (calcd. for  $\text{C}_{23}\text{H}_{37}\text{NO}_3\text{S}$ , 407.XXX).

(38): colorless amorphous solid;  $[\alpha]^{22}_{\text{D}} +25.0$  ( $c$  0.5, MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 212 (17700), 247 (13400); IR (KBr)  $\nu_{\text{max}}$  3427, 2971, 2933, 2878, 2858, 1709, 1457, 1377, 1186, 1023  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz)  $\delta$  6.95 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.52 (1H, dtt,  $J$  = 10.9, 7.2, 1.4 Hz, H-12), 5.39 (1H, dtt,  $J$  = 10.9, 7.1, 1.2 Hz, H-13), 4.18 (1H, ddt,  $J$  = 3.4, 0.4, 6.7 Hz, H-15), 2.71 (3H, s, H-21), 2.51 (1H, bq,  $J$  = 6.8 Hz, H-8), 2.48 (1H, dq,  $J$  = 17.7, 7.4 Hz, H-6a), 2.41 (1H, dq,  $J$  = 17.7, 7.2 Hz, H-6b), 2.39 (2H, ddd,  $J$  = 7.1, 6.7, 1.4 Hz, H-14), 2.06 (2H, ddt, 7.2, 1.2, 7.0 Hz, H-11), 2.05 (3H, d,  $J$  = 1.4 Hz, H-27), 1.81 (1H, d,  $J$  = 3.4 Hz,

15-OH), 1.66 (1H, m, H-9a), 1.32 (1H, m, H-9b), 1.31 (2H, m, H-10), 1.06 (3H, d,  $J = 6.9$  Hz, H-25), 1.04 (3H, dd,  $J = 7.4, 7.2$  Hz, H-24);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz)  $\delta$  215.3 (s, C-7), 164.6 (s, C-20), 152.9 (s, C-18), 141.5 (s, C-16), 132.7 (d, C-12), 125.3 (d, C-13), 119.2 (d, C-17), 115.6 (d, C-19), 77.2 (d, C-15), 46.0 (d, C-8), 34.3 (t, C-14), 33.5 (t, C-6), 32.7 (t, C-9), 27.5 (t, C-11), 27.3 (t, C-10), 19.2 (q, C-21), 16.5 (q, C-25), 14.4 (q, C-27), 7.8 (q, C-24); EIMS  $m/z$  335 [M]<sup>+</sup> (2), 317 (4), 170 (27), 169 (67), 168 (100), 140 (20); HREIMS  $m/z$  335.1912 (calcd. for  $\text{C}_{19}\text{H}_{29}\text{NO}_2\text{S}$ , 335.1919).

(39): colorless amorphous solid;  $[\alpha]^{22}_D +26.4$  ( $c 0.27$ , MeOH); UV (MeOH)  $\lambda_{\text{max}}$  nm ( $\epsilon$ ) 203 (19100), 244 (12500); IR (KBr)  $\nu_{\text{max}}$  3430, 2970, 2934, 2877, 1710, 1458, 1377, 1184  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz)  $\delta$  6.94 (1H, s, H-19), 6.55 (1H, bs, H-17), 5.17 (1H, t,  $J = 7.3$  Hz, H-13), 4.13 (1H, m, H-15), 2.70 (3H, s, H-21), 2.51 (1H, bq,  $J = 6.8$  Hz, H-8), 2.47 (1H, dq,  $J = 17.7, 7.2$  Hz, H-6a), 2.41 (1H, dq,  $J = 17.7, 7.2$  Hz, H-6b), 2.33 (2H, bdd,  $J = 7.3, 6.8$  Hz, H-14), 2.05 (3H, d,  $J = 1.2$  Hz, H-27), 2.03 (2H, m, H-11), 1.71 (1H, d,  $J = 3.2$  Hz, 15-OH), 1.69 (3H, d,  $J = 1.3$  Hz, H-26), 1.62 (1H, m, H-9a), 1.32 (3H, m, H-10 and H-9b), 1.06 (3H, d,  $J = 6.9$  Hz, H-25), 1.03 (3H, t,  $J = 7.2$  Hz, H-24); EIMS  $m/z$  349 [M]<sup>+</sup> (0.7), 331 (1.7), 168 (100), 140 (5.1); HREIMS  $m/z$  349.XXX (calcd. for  $\text{C}_{20}\text{H}_{31}\text{NO}_2\text{S}$ , 349.XXX).

Tab 1. Aktivität von Epothilonen und Verbindungen (1) bis (39) gegen Maus-Fibroblasten (L929, IC<sub>50</sub> /ng/ml/)

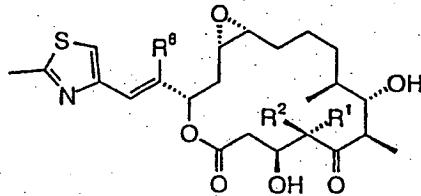
Struktur-typ	Epothilone				
	A <sub>V</sub>	B <sub>V</sub>	C <sub>V</sub>	D <sub>V</sub>	trans C <sub>V</sub>
<b>Ausgangs-epothilon</b>	(1) 4	(2) 1-2	(14) 50-100	(15) 20	-
21-Hydroxy (E&F)	(3) 10	(4) 1.5	-	-	-
Oxazoles (G&H)	(10) 6	(11) 1	(12) 120	(13) 11	-
(R)-4-Desmethyl (X <sub>1</sub> )	(5) 20	-	(16) 200	(17) 20	(28) 400
(S)-4-Desmethyl (X <sub>2</sub> )	(6) 7	-	(18) 25-30	(19) 12	(29) 80
6-Desmethyl (X <sub>3</sub> )	-	-	(20) 1500	-	-
8-Desmethyl (X <sub>4</sub> )	-	-	(21) 800	-	-
8,9-Dehydro (X <sub>5</sub> )	-	-	(22) 1500	(23) 200	-
10,11-Dehydro (X <sub>6</sub> )	-	-	(24) 120	-	-
14-Hydroxy (X <sub>7</sub> )	-	-	(25)	-	-
16-Desmethyl (X <sub>8</sub> )	(7) 20	-	(26) 250	-	-
27-Hydroxy (X <sub>9</sub> )	(8) 100	-	(27) 200	-	-
21-Methyl (X <sub>10</sub> )	-	(9) 1.5	-	-	-
Verbindung	-	-	(36) 180	-	-
Verbindung	-	-	(37) 50	-	-
Verbindung	-	-	(38) 2000	(39) 500	-

## Epothilon-Nebenkomponenten

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### Patentansprüche

#### 1. Epothilon der Formel



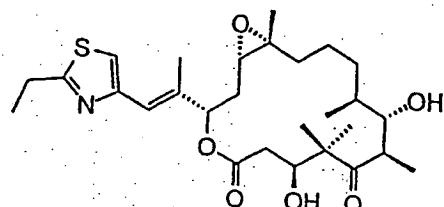
Epothilone A<sub>1</sub> (5) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>8</sup> = Me

Epothilone A<sub>2</sub> (6) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>8</sup> = Me

Epothilone A<sub>3</sub> (7) R<sup>8</sup> = H; R<sup>1</sup>, R<sup>2</sup> = Me oder

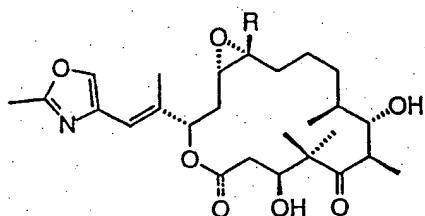
Epothilone A<sub>4</sub> (8) R<sup>1</sup> = CH<sub>2</sub>OH; R<sup>2</sup>, R<sup>8</sup> = Me

#### 2. Epothilon der Formel



Epothilone B<sub>10</sub> (9)

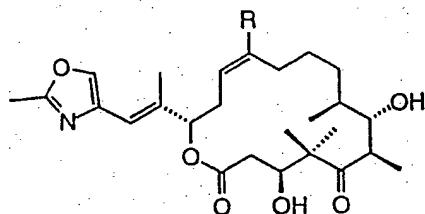
## 3. Epothilon der Formel



✓ Epothilone G<sub>1</sub> (10) R = H  
 ✓ Epothilone G<sub>2</sub> (11) R = Me

oder

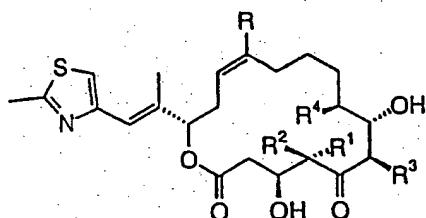
## 4. Epothilon der Formel



✓ Epothilone H<sub>1</sub> (12) R = H  
 ✓ Epothilone H<sub>2</sub> (13) R = Me

oder

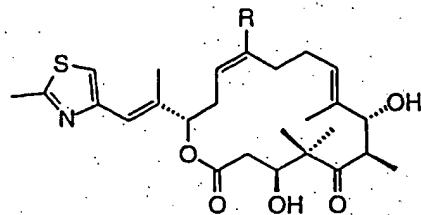
## 5. Epothilon der Formel



✓ Epothilone C<sub>1</sub> (16) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = H  
 ✓ Epothilone D<sub>1</sub> (17) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = Me  
 ✓ Epothilone C<sub>2</sub> (18) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = H  
 ✓ Epothilone D<sub>2</sub> (19) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>3</sup>, R<sup>4</sup> = Me; R = Me  
 ✓ Epothilone C<sub>3</sub> (20) R<sup>3</sup> = H; R<sup>1</sup>, R<sup>2</sup>, R<sup>4</sup> = Me; R = H  
 ✓ Epothilone C<sub>4</sub> (21) R<sup>4</sup> = H; R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> = Me; R = H

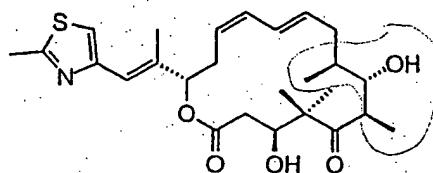
oder

## 6. Epothilon der Formel

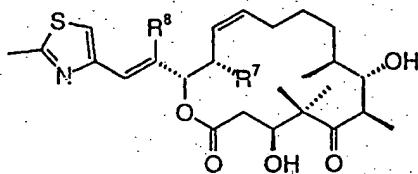
Epothilone C<sub>5</sub> (22) R = HEpothilone D<sub>5</sub> (23) R = Me

oder

## 7. Epothilon der Formel

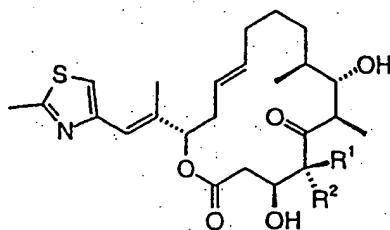
✓ Epothilone C<sub>6</sub> (24)

## 8. Epothilin der Formel

✓ Epothilone C<sub>7</sub> (25) R<sup>7</sup> = OH; R<sup>8</sup> = Me✓ Epothilone C<sub>8</sub> (26) R<sup>8</sup>, R<sup>7</sup> = H✓ Epothilone C<sub>9</sub> (27) R<sup>8</sup> = CH<sub>2</sub>OH; R<sup>7</sup> = H

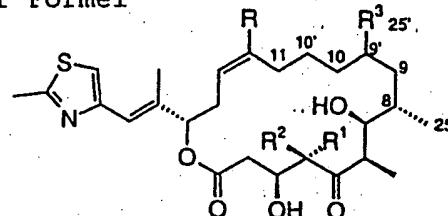
oder

## 9. Epothilon der Formel

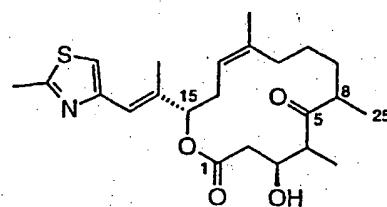
✓ trans-Epothilone C<sub>1</sub> (28) R<sup>1</sup> = H; R<sup>2</sup> = Me✓ trans-Epothilone C<sub>2</sub> (29) R<sup>2</sup> = H; R<sup>1</sup> = Me

oder

## 10. Epothilon der Formel

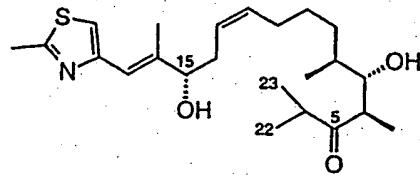
Epothilone I<sub>1</sub> (30) R, R<sup>3</sup> = H; R<sup>1</sup>, R<sup>2</sup> = MeEpothilone I<sub>2</sub> (31) R = H; R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup> = MeEpothilone I<sub>3</sub> (32) R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R = MeEpothilone I<sub>4</sub> (33) R<sup>2</sup>, R = H; R<sup>1</sup>, R<sup>3</sup> = MeEpothilone I<sub>5</sub> (34) R<sup>2</sup> = H; R<sup>1</sup>, R<sup>3</sup>, R = Me oderEpothilone I<sub>6</sub> (35) R<sup>1</sup> = H; R<sup>2</sup>, R<sup>3</sup>, R = Me

## 11. Epothilon der Formel



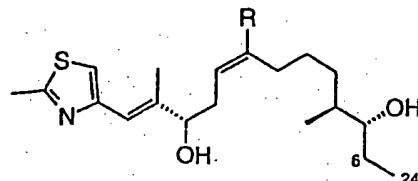
✓ Epothilone K (36)

## 12. Verbindung der Formel



(37)

## 13. Verbindung der Formel



(38) R = H

oder

(39) R = Me

1/2

Fig. 1

## Trennungsgang für

## Rohepothilone

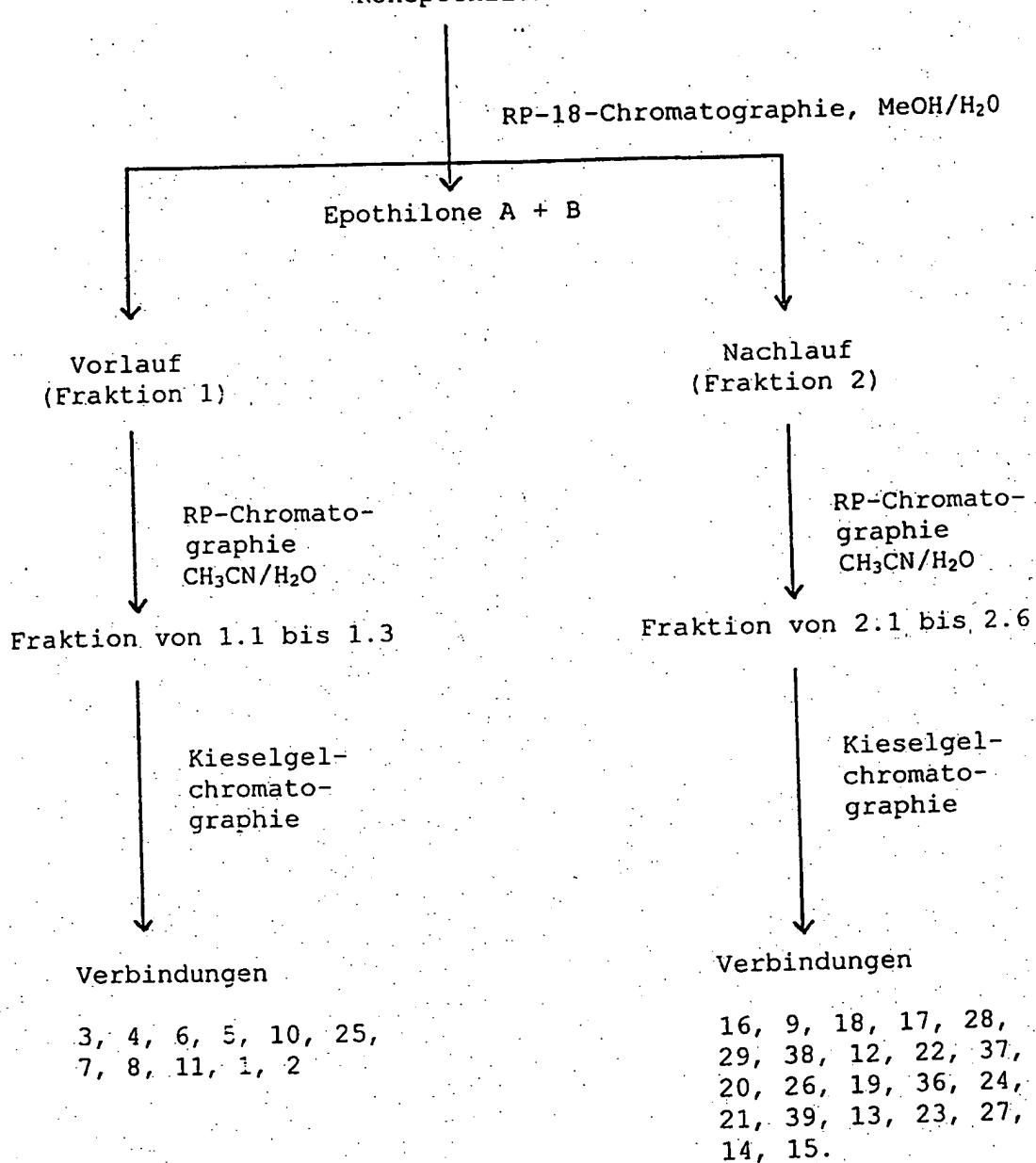


Fig. 2

fraction 1	Epothilone E (3)	variable <sup>a</sup>
	Epothilone F (4)	variable <sup>a</sup>
	Epothilone A <sub>2</sub> (6)	14.5 mg
	Epothilone A <sub>1</sub> (5)	3.1 mg
	Epothilone G <sub>1</sub> (10)	62.3 mg
	Epothilone C <sub>7</sub> (25)	0.9 mg
	Epothilone A <sub>4</sub> (7)	38.7 mg
	Epothilone A <sub>5</sub> (8)	4.4 mg
	Epothilone G <sub>2</sub> (11)	9.4 mg
	Epothilone A (1)	29800.0 mg
fraction 2	Epothilone B (2)	10300.0 mg
	Epothilone C <sub>1</sub> (16)	32.4 mg
	Epothilone B <sub>10</sub> (9)	1.1 mg
	Epothilone C <sub>2</sub> (18)	58.4 mg
	Epothilone D <sub>1</sub> (17)	5.3 mg
	trans-Epothilone C <sub>1</sub> (28)	1.4 mg
	trans-Epothilone C <sub>2</sub> (29)	4.5 mg
	38	6.5 mg
	Epothilone H <sub>1</sub> (12)	3.0 mg
	Epothilone C <sub>6</sub> (22)	7.3 mg
	37	2.8 mg
	Epothilone C <sub>3</sub> (20)	32.5 mg
	Epothilone C <sub>8</sub> (26)	26.3 mg
	Epothilone D <sub>2</sub> (19)	13.1 mg
2.6	Epothilone K (36)	0.4 mg
	Epothilone C <sub>5</sub> (24)	2.9 mg
	Epothilone C <sub>4</sub> (21)	6.5 mg
	39	0.8 mg
	Epothilone H <sub>2</sub> (13)	1.5 mg
	Epothilone D <sub>5</sub> (23)	0.9 mg
	Epothilone C <sub>9</sub> (27)	3.0 mg
	Epothilone C (14)	4600.0 mg
	Epothilone D (15)	2700.0 mg

PCT

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INTERNATIONALE ANMELDUNG VERÖFFENTLICH NACH DEM VERTRAG ÜBER DIE  
INTERNATIONALE ZUSAMMENARBEIT AUF DEM GEBIET DES PATENTWESENS (PCT)



(51) Internationale Patentklassifikation <sup>6</sup> : <b>C07D 493/04, 417/06, 413/06, 277/24</b> <b>// (C07D 493/04, 313:00, 303:00)</b>		A3	(11) Internationale Veröffentlichungsnummer: <b>WO 99/65913</b>
			(43) Internationales Veröffentlichungsdatum: <b>23. Dezember 1999 (23.12.99)</b>
(21) Internationales Aktenzeichen: <b>PCT/EP99/04244</b>		(81) Bestimmungsstaaten: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO Patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), eurasisches Patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), europäisches Patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI Patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(22) Internationales Anmeldedatum: <b>18. Juni 1999 (18.06.99)</b>			
(30) Prioritätsdaten: <b>198 26 988.9 18. Juni 1998 (18.06.98) DE</b>			
(71) Anmelder ( <i>für alle Bestimmungsstädte ausser US</i> ): <b>GESELLSCHAFT FÜR BIOTECHNOLOGISCHE FORSCHUNG MBH (GBF) [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE).</b>			
(72) Erfinder; und		Veröffentlicht	
(75) Erfinder/Anmelder ( <i>nur für US</i> ): <b>HOEFLE, Gerhard [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). REICHENBACH, Hans [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). GERTH, Klaus [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). HARDT, Ingo [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). SASSE, Florenz [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE). STEINMETZ, Heinrich [DE/DE]; Mascheroder Weg 1, D-38124 Braunschweig (DE).</b>		<i>Mit internationalem Recherchenbericht. Vor Ablauf der für Änderungen der Ansprüche zugelassenen Frist. Veröffentlichung wird wiederholt falls Änderungen eintreffen.</i>	
(74) Anwälte: <b>BOETERS, Hans usw.; Boeters &amp; Bauer, Bereiteranger 15, D-81541 München (DE).</b>		(88) Veröffentlichungsdatum des internationalen Recherchenberichts: <b>20. April 2000 (20.04.00)</b>	

(54) Title: EPOTHILONE MINOR CONSTITUENTS

(54) Bezeichnung: EPOTHILON-NEBENKOMPONENTEN

(57) Abstract

The invention relates to compounds which are obtained by fermenting DSM 6773, especially epothilones A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 and K and trans-epothilones C1 and C2.

(57) Zusammenfassung

Die Erfindung betrifft Verbindungen, die durch Fermentation von DSM 6773 erhältlich sind, insbesondere Epothilone A1, A2, A8, A9, B10, C1, C2, C3, C4, C5, C6, C7, C8, C9, D1, D2, D5, G1, G2, H1, H2, I1, I2, I3, I4, I5, I6 und K und Trans-Epothilone C1 und C2.

**LEDIGLICH ZUR INFORMATION**

Codes zur Identifizierung von PCT-Vertragsstaaten auf den Kopfbögen der Schriften, die internationale Anmeldungen gemäss dem PCT veröffentlichen.

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# INTERNATIONAL SEARCH REPORT

International application No  
PCT/EP 99/04244

**A. CLASSIFICATION OF SUBJECT MATTER**  
**IPC 6 C07D493/04 C07D417/06 C07D413/06 C07D277/24**  
**//(C07D493/04, 313:00, 303:00)**

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)  
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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
<input checked="" type="checkbox"/>	WO 98 08849 A (NOVARTIS AKTIENGESELLSCHAFT ;BAUER ARMIN (DE); CORDES MARTIN (DE);) 5 March 1998 (1998-03-05) abstract; claims; examples	1-13
<input checked="" type="checkbox"/>	WO 98 22461 A (BIOTECHNOLOG FORSCHUNG GMBH ;GERTH KLAUS (DE); HOEFLER GERHARD (DE)) 28 May 1998 (1998-05-28) abstract; claims; examples	1-13
<input checked="" type="checkbox"/>	WO 97 19086 A (BIOTECHNOLOG FORSCHUNG GMBH ;KIFFE MICHAEL (DE); HOEFLER GERHARD (D) 29 May 1997 (1997-05-29) abstract; claims; examples	1-13
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Further documents are listed in the continuation of box C.

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Date of the actual completion of the International search

Date of mailing of the International search report

22 February 2000

07/03/2000

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Paisdor, B

**INTERNATIONAL SEARCH REPORT**

International Application No  
PCT/EP 99/04244

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>NICOLAOU K C ET AL: "DESIGNED EPOTHILONES: COMBINATORIAL SYNTHESIS, TUBULIN ASSEMBLY PROPERTIES, AND CYTOTOXIC ACTION AGAINST TAXOL RESISTANT TUMOR CELLS"            ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, DE, VERLAG CHEMIE. WEINHEIM, vol. 36, no. 19, 1 January 1997 (1997-01-01), pages 2097-2103, XP002064441            ISSN: 0570-0833            page 2099 -page 2100</p>	1-13
X	<p>NICOLAOU ET AL: "Total synthesis of oxazole- and cyclopropane-containing epothilone A analogs by the olefin metathesis approach"            CHEMISTRY - A EUROPEAN JOURNAL, US, VCH PUBLISHERS, vol. 3, no. 12, 1997, pages 1957-1970, XP002121565            ISSN: 0947-6539            page 1959 -page 1961</p>	1-13
X	<p>BALOG A ET AL: "Stereoselective Syntheses and Evaluation of Compounds in the 8-Desmethylepothilone A Series: Some Surprising Observations Regarding Their Chemical and Biological Properties"            TETRAHEDRON LETTERS, NL, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, vol. 38, no. 26, 30 June 1997 (1997-06-30), pages 4529-4532, XP004074826            ISSN: 0040-4039            the whole document</p>	1-13
X	<p>SU D -S ET AL: "STRUCTURE - ACTIVITY RELATIONSHIPS OF THE EPOTHILONES AND THE FIRST IN VIVO COMPARISON WITH PACLITAXEL"            ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, DE, VERLAG CHEMIE. WEINHEIM, vol. 36, no. 19, 1997, pages 2093-2096, XP002916075            ISSN: 0570-0833            page 2094 -page 2095</p>	1-13
	-/-	

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 99/04244

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	K.C. NICOLAOU ET AL.: "Probing the ring size of epothilones: total synthesis of '14!-, '15!-, '17!-, and '18!Epothilones A" ANGEWANDTE CHEMIE INTERNATIONAL EDITION., vol. 37, no. 1/2, 1998, pages 81-84, XP002131226 WEINHEIM DE the whole document	1-13

**INTERNATIONAL SEARCH REPORT**

Information on patent family members.

International application No
PCT/EP 99/04244

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
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		DE	19645362 A	30-04-1998
		AU	2149397 A	19-03-1998
		EP	0923583 A	23-06-1999
		US	5969145 A	19-10-1999
WO 9822461	A 28-05-1998	AU	5483798 A	10-06-1998
		CZ	9901750 A	15-09-1999
		EP	0941227 A	15-09-1999
		NO	992338 A	14-05-1999
		PL	333435 A	06-12-1999
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		DE	19639456 A	26-03-1998
		EP	0873341 A	28-10-1998
		EP	0903348 A	24-03-1999

# INTERNATIONALER RECHERCHENBERICHT

Internat. Aktenzeichen  
PCT/EP 99/04244

**A. KLASIFIZIERUNG DES ANMELDUNGSGEGENSTANDES**  
**IPK 6 C07D493/04 C07D417/06 C07D413/06 C07D277/24**  
**//(C07D493/04, 313:00, 303:00)**

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Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	WO 98 08849 A (NOVARTIS AKTIENGESELLSCHAFT ; BAUER ARMIN (DE); CORDES MARTIN (DE);) 5. März 1998 (1998-03-05) Zusammenfassung; Ansprüche; Beispiele	1-13
X	WO 98 22461 A (BIOTECHNOLOG FORSCHUNG GMBH ; GERTH KLAUS (DE); HOEFLER GERHARD (DE)) 28. Mai 1998 (1998-05-28) Zusammenfassung; Ansprüche; Beispiele	1-13
X	WO 97 19086 A (BIOTECHNOLOG FORSCHUNG GMBH ; KIFFE MICHAEL (DE); HOEFLER GERHARD (D)) 29. Mai 1997 (1997-05-29) Zusammenfassung; Ansprüche; Beispiele	1-13
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**INTERNATIONALER RECHERCHENBERICHT**

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**C.(Fortsetzung) ALS WESENTLICH ANGEBEHENE UNTERLAGEN**

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	<p>NICOLAOU K C ET AL: "DESIGNED EPOTHILONES: COMBINATORIAL SYNTHESIS, TUBULIN ASSEMBLY PROPERTIES, AND CYTOTOXIC ACTION AGAINST TAXOL RESISTANT TUMOR CELLS".            ANGEWANDTE CHEMIE. INTERNATIONAL EDITION, DE, VERLAG CHEMIE. WEINHEIM, Bd. 36, Nr. 19, 1. Januar 1997 (1997-01-01), Seiten 2097-2103, XP002064441            ISSN: 0570-0833            Seite 2099 -Seite 2100</p>	1-13
X	<p>NICOLAOU ET AL: "Total synthesis of oxazole- and cyclopropane-containing epothilone A analogs by the olefin metathesis approach"            CHEMISTRY - A EUROPEAN JOURNAL, US, VCH PUBLISHERS, Bd. 3, Nr. 12, 1997, Seiten 1957-1970, XP002121565            ISSN: 0947-6539            Seite 1959 -Seite 1961</p>	1-13
X	<p>BALOG A ET AL: "Stereoselective Syntheses and Evaluation of Compounds in the 8-Desmethylepothilone A Series: Some Surprising Observations Regarding Their Chemical and Biological Properties"            TETRAHEDRON LETTERS, NL, ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, Bd. 38, Nr. 26, 30. Juni 1997 (1997-06-30), Seiten 4529-4532, XP004074826            ISSN: 0040-4039            das ganze Dokument</p>	1-13
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**INTERNATIONALER RECHERCHENBERICHT**

Internation	Aktenzeichen
PCT/EP 99/04244	

**C.(Fortsetzung) ALS WESENTLICH ANGESEHENE UNTERLAGEN**

Kategorie*	Bezeichnung der Veröffentlichung, soweit erforderlich unter Angabe der in Betracht kommenden Teile	Betr. Anspruch Nr.
X	<p>K.C. NICOLAOU ET AL.: "Probing the ring size of epothilones: total synthesis of '14!-, '15!-, '17!-, and '18!Epothilones A"  <b>ANGEWANDTE CHEMIE INTERNATIONAL EDITION.</b>,          Bd. 37, Nr. 1/2, 1998, Seiten 81-84,          XP002131226  <b>WEINHEIM DE</b>          das ganze Dokument</p> <hr/>	1-13

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Angaben zu Veröffentlichungen, die zur selben Patentfamilie gehören

Internat:	Aktenzeichen
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